(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 May 2001 (17.05.2001)

PCT

(10) International Publication Number
WO 01/34573 A1

(51) International Patent Classification[7]: C07D 235/28, A61K 31/4184, A61P 1/04

(21) International Application Number: PCT/SE00/02192

(22) International Filing Date:
8 November 2000 (08.11.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9904044-6 9 November 1999 (09.11.1999) SE

(71) Applicant *(for all designated States except US)*: **PHARMACIA AB** [SE/SE]; S-112 87 Stockholm (SE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **ABEDI, Joseph** [GH/US]; 17A Arlington Street, Cambridge, MA 02140 (US). **CARCANAGUE, Daniel** [US/US]; AstraZeneca R & D Boston, 35 Gatehouse Drive, Waltham, MA 02451 (US). **KÜHLER, Thomas** [SE/SE]; AstraZeneca R & D Mölndal, S-431 83 Mölndal (SE). **SHUE, Youe-Kong** [US/US]; 7869 Via Teca, Carlsbad, CA 92009 (US). **WUONOLA, Mark** [US/US]; AstraZeneca R & D Boston, 35 Gatehouse Drive, Waltham, MA 02451 (US).

(74) Agent: **ASTRAZENECA AB**; Global Intellectual Property, S-151 85 Södertälje (SE).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

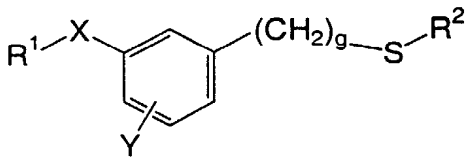
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*
— *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/34573 A1

(54) Title: COMPOUNDS



(I)

(57) Abstract: The invention relates to compounds of formula (I) which have anti-*Helicobacter pylori* activity.

COMPOUNDS

The present invention relates to compounds which have anti-*Helicobacter pylori* activity, i.e., compounds which can be administered to a mammalian patient therapeutically to treat *Helicobacter pylori* infection in the patient. The invention also relates to pharmaceutical formulations, use of a compound of the invention in the manufacture of a medicament, and processes for preparing the compounds.

Background to the Invention

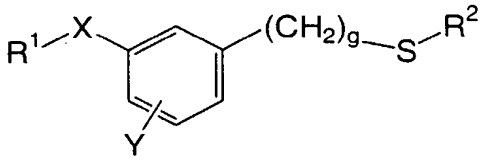
Helicobacter pylori is a gram negative bacterium which infects the human gastric mucosa. Infection with the bacterium causes inflammation of the gastric mucosa. Peptic ulceration of the duodenum or stomach can develop as well as adenocarcinomas or lymphomas of the stomach wall. Omeprazole (5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1*H*-benzimidazole) is active against *Helicobacter pylori* (see Vogt, K and Hahn, H (1998), "Bactericidal Activity of Lansoprazole and Omeprazole against Helicobacter pylori in vitro", Drug Res. 48(1), No. 6, 694-697), and is labile towards rearrangement in acidic media. Omeprazole is a sulfoxide. This sulfoxide is labile towards rearrangement in acidic media and the rearrangement gives an intermediate, which is a potent proton pump inhibitor. Thus, the parent compound does not persist in the acidic environment of the stomach. Compounds related to omeprazole, where the sulphur atom is unoxidized are also active against *Helicobacter pylori*. However, these related compounds can undergo metabolic oxidation *in vivo* to give the corresponding sulfoxide, analagous to omeprazole, and have a propensitiy towards rearrangement in acidic media *in vivo* [J. Med. Chem. **1988**, *41*, 1777-1788]. Analogues which are potent against *Helicobacter pylori*, but not acid labile and thus stable in acidic media are desirable. Such analogues could be administered to a mammalian patient therapeutically to treat *Helicobacter pylori* infection.

In addition, it would be preferable for such analogues to be selective for *Helicobacter pylori*, since this is desirable to avoid the disruption of the normal gastrointestinal flora, and to reduce the incidence of bacterial resistance development.

Summary of the Invention

Accordingly, the present invention provides compounds of formula I or pharmaceutically acceptable salts or solvates thereof which are active against *Helicobacter pylori*, but lack the pyridine nitrogen of omeprazole and its analogues which is necessary for

rearrangement in acidic media. Thus, the compounds of the invention are more stable in acid media. Formula I is as follows:



I

wherein:

X is S; SO_2; NH; N(C_{1-6}alkyl); O or CH_2;

Y is C_{1-6}alkyl; O(C_{3-8}cycloalkyl); O(C_{1-6}alkyl); Hal; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal , wherein Hal represents halogen; NRR´, wherein R and R´ independently represent H or C_{1-8}alkyl, or NRR´ represents an optionally substituted C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S; H; COOR″ or COR″, R″ representing H or C_{1-6}alkyl; or CH_2OH;

R^1 $-(CH_2)_a-R^3$; $-((CH_2)_bO)_c-R^3$; $-(CH_2)_d-R^{3'}$; $-(CH_2)_aC(=O)R^3$; $-(CH_2)_dC(=O)R^{3'}$; $-((CH_2)_e-O)_{c'}-(CH_2)_f-R^{3'}$; R^3 or $R^{3'}$.

R^2 is an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S;

R^3 is H; C_{1-6}alkyl; optionally substituted C_{3-8}cycloalkyl optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or an optionally substituted 5- to 10-membered mono- or bi-cyclic heterocyclic ring structure containing 1, 2, 3, 4 or 5 heteroatoms independently selected from O, N and S;

$R^{3'}$ is -Z-M wherein Z represents O, S or NH and M represents H, an optionally substituted mono- or bi- cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, or an optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or -Z-M represents $-C(=O)NR^6R^7$, $-NR^6R^7$, $-OC(=O)NR^8R^9$, $-NC(=O)NR^8R^9$ or $-NC(=O)R^8$;

For R^4 and R^5, either:

(i) R^4 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; Z^2-(C_{1-8}alkyl)aryl, wherein Z^2 represents O or a bond, and the aryl is C6-10, optionally substituted and optionally fused to a C_{5-10} heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted C_{6-10}aryl; an

optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2 or 3 heteroatoms independently selected from O, N and S; (C_{1-8}alkyl)-R, wherein R represents an optionally substituted mono- or bi-cyclic 5 to 10 membered heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted -C(=O)O(C_{1-8}alkyl); optionally substituted -C(=O)O-phenyl; optionally substituted -C(=O)(C_{1-8}alkyl); optionally substituted -C(=O)-phenyl; or -NC(=O)R^6 and

R^5 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10} and optionally substituted; optionally substituted C_{6-10}aryl; or an optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or

(ii) the structure -NR^4R^5 represents a C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S and optionally fused to a C_{6-10} ring structure, -NR^4R^5 being optionally substituted;

For R^6 and R^7, either:

(i) R^6 is H; C_{1-12}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; optionally substituted (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10}; optionally substituted (C_{1-8}alkyl)R, where R represents a mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S or R represents a mono-, bi- or tri-cyclic C_{3-13}cycloalkyl; optionally substituted C_{6-10}aryl; an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; or -C(=O)O-Ar, wherein Ar represents optionally substituted C_{6-10}aryl; and R^7 is H; or

(ii) the structure -NR^6R^7 represents a C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S, -NR^6R^7 being optionally substituted;

a represents an integer 1, 2, 3, 4 or 5;

each b independently represents an integer 1, 2, 3, 4 or 5;

c represents an integer 1, 2, 3, 4 or 5;

c' represents an integer 1, 2, 3, 4 or 5;

d represents an integer 1, 2, 3, 4 or 5;

each e independently represents an integer 1, 2, 3, 4 or 5;

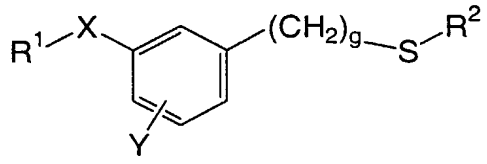
f represents an integer 1, 2, 3, 4 or 5; and

g represents zero or an integer 1, 2, 3, 4 or 5.

The invention also relates to pharmaceutical formulations, use of a compound of the invention in the manufacture of a medicament, processes for preparing the compounds and intermediates for use in such processes.

Detailed Description of the Invention

The present invention provides a compound of formula I or a pharmaceutically acceptable salt or solvate thereof



I

wherein:

X represents S; SO_2; NH; O or CH_2. Alternatively, X represents $N(C_{1-6}alkyl)$, more preferably N-methyl or $N(C_{2-4}alkyl)$.

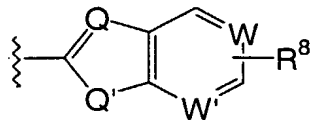
Y represents $C_{1-6}alkyl$ (preferably $C_{2-4}alkyl$, and most preferably methyl); $O(C_{3-8}cycloalkyl)$, preferably O-cyclopropyl, or O-cyclobutyl or O-cyclopentyl; $O(C_{1-6}alkyl)$, preferably Omethyl or $O(C_{2-4}alkyl)$; Hal, preferably Cl or F; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal , wherein Hal represents halogen (preferably F); NRR´, wherein R and R´ independently represent H or $C_{1-8}alkyl$ (preferably methyl or $C_{2-6}alkyl$ or $C_{2-4}alkyl$) , or NRR´ represents an optionally substituted C_{3-8}, preferably C_{3-6}, heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S; H; COOR″ or COR″, R″ representing H or $C_{1-6}alkyl$ (preferably methyl, ethyl); or CH_2OH. For optional substitution of the heterocyclic ring represented by NRR´, at least one (e.g., one, two or three) substituents may be provided independently selected from $C_{1-6}alkyl$ (preferably $C_{2-4}alkyl$, more preferably methyl); phenyl; OCF_3; $OCHF_2$; $-O(C_{1-8}alkyl)$, preferably -O-methyl, -O-ethyl or $-O(C_{3-6}alkyl)$; $-C(=O)O(C_{1-8}alkyl)$, preferably -C(=O)O-methyl, -C(=O)O-ethyl, -C(=O)O-*tert*-butyl or $-C(=O)O(C_{3-6}alkyl)$; -C(=O)O-phenyl; -O-phenyl; $-C(=O)(C_{1-8}alkyl)$, preferably -C(=O)-methyl, -C(=O)-ethyl or $-C(=O)(C_{3-6}alkyl)$; -C(=O)OH; $-S(C_{1-8}alkyl)$, preferably -S-methyl, -S-ethyl or $-S(C_{3-6}alkyl)$; OH; halogen (e.g., F, Cl or Br); NRR' where R and R' are independently H or $C_{1-6}alkyl$ (preferably $C_{2-4}alkyl$, more preferably methyl, most preferably R=R'=methyl); and nitro.

R^1 represents $-(CH_2)_a-R^3$; $-((CH_2)_bO)_c-R^3$; $-(CH_2)_d-R^{3'}$; $-((CH_2)_e-O)_{c'}-(CH_2)_f-R^{3'}$ (preferably where e=2 and f=2); R^3 or $R^{3'}$. Preferably, R^1 represents $-(CH_2)_a-CH_3$ or

-$((CH_2)_bO)_c$-CH_3. More preferably, R^1 is selected from –*iso*-Bu; -$(CH_2CH_2O)_3CH_3$; -(CH_2CH_2)-4-morpholinyl; -$(CH_2CH_2O)_5CH_3$; -(CH_2CH_2)-1-(2-methyl-5-nitro-imidazolyl); -(CH_2CH_2)-1-(1,2,4-triazolyl); and –(CH_2CH_2)-OC(=O)NH-Ph.

R^2 represents an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S. Preferred examples of the heterocycle are benzimidazolyl (preferably benzimidazol-2-yl), imidazolyl (preferably imidazol-2-yl), oxadiazolyl (preferably 1,3,4-oxadiazol-2-yl), pyrimidinyl (preferably pyrimidin-2-yl), tetrazolyl (preferably 1,2,3,4-tetrazol-5-yl), pyridinyl (preferably pyridin-2-yl or pyridin-4-yl), thiazolyl (preferably 1,3-thiazol-2-yl), pyridineimidazolyl (preferably pyridineimidazol-2-yl), benzoxazolyl (preferably 1,3-benzoxazol-2-yl), indolyl (preferably indol-2-yl). For optional substitution of the heterocycle, at least one (e.g., one, two or three) substituents may be provided independently selected from nitro; carboxylate; -COOH; =O; -S(=O)-(C_{1-8}alkyl), the alkyl preferably being methyl, ethyl or C_{3-6}alkyl; -S(=O)-(=O)-(C_{1-8}alkyl), the alkyl preferably being methyl, ethyl or C_{3-6}alkyl; halogen (preferably F or Cl); phenyl;
-O(C_{1-8}alkyl), preferably -O-methyl, -O-ethyl or -O(C_{3-6}alkyl); -S(C_{1-8}alkyl), preferably -S-methyl, -S-ethyl or -S(C_{3-6}alkyl); OH; $OCHF_2$, OCH_2F, OCF_3; CHF_2, CH_2F, CF_3;
-C(=O)NRR′, wherein R and R′ are independently selected from H and C_{1-8}alkyl (preferably methyl, ethyl, propyl, isopropyl, or C_{2-6}alkyl), or the structure NRR′ represents an optionally substituted C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S; and
- R″-NH(CO) R‴, wherein R″ represents C_{1-6}alkylene (preferably C_1 or C_2) and R‴ represents C_{1-6}alkyl (preferably C_1 or C_2).

In one preferred embodiment, R^2 represents



wherein:

Q is CH or N;

Q′ is NH, O or S;

W is CH or N;

W′ is CH or N; and

R^8 represents C_{1-6}alkyl (preferably C_{2-4}alkyl, and most preferably methyl); O(C_{3-8}cycloalkyl), preferably O-cyclopropyl, or O-cyclobutyl or O-cyclopentyl; O(C_{1-6}alkyl), preferably Omethyl or O(C_{2-4}alkyl); Hal, preferably Cl or F; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal, wherein Hal represents halogen (preferably F); NRR´, wherein R and R´ independently represent H or C_{1-8}alkyl (preferably methyl or C_{2-6}alkyl or C_{2-4}alkyl) , or NRR´ represents an optionally substituted C_{3-8}, preferably C_{3-6}, heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S; H; $COOR^9$ or COR^9, R^9 representing H or C_{1-6}alkyl (preferably methyl, ethyl); or CH_2OH. For optional substitution of the heterocyclic ring represented by NRR´, at least one (e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl); phenyl; OCF_3; $OCHF_2$; -O(C_{1-8}alkyl), preferably -O-methyl, -O-ethyl or -O(C_{3-6}alkyl); -C(=O)O(C_{1-8}alkyl), preferably -C(=O)O-methyl, -C(=O)O-ethyl, -C(=O)O-*tert*-butyl or -C(=O)O(C_{3-6}alkyl); -C(=O)O-phenyl; -O-phenyl; -C(=O) (C_{1-8}alkyl), preferably -C(=O)-methyl, -C(=O)-ethyl or -C(=O)(C_{3-6}alkyl) ; -C(=O)OH; -S(C_{1-8}alkyl), preferably -S-methyl, -S-ethyl or -S(C_{3-6}alkyl); OH; halogen (e.g., F, Cl or Br), NRR' where R and R' are independently H or C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl, most preferably R=R'=methyl); and nitro.

R^3 represents H; C_{1-6}alkyl; optionally substituted C_{3-8}, preferably C_{3-6}, cycloalkyl optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; optionally substituted C_{5-10}aromatic ring structure (e.g., phenyl) optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or an optionally substituted 5- to 10-membered mono- or bi-cyclic heterocyclic ring structure containing 1, 2, 3, 4 or 5 heteroatoms independently selected from O, N and S. Preferably, the cycloalkyl contains heteroatoms and is selected from morpholinyl (4-morpholinyl), piperazinyl (preferably 1-piperazinyl), tetrazolyl (preferably 1,2,3,4-tetrazol-2-yl), imidazolyl (e.g., 1-imidazolyl) and triazolyl (e.g., 1-(1,2,4-triazolyl)). Preferred examples of the C_{1-6}alkyl are preferably C_{2-4}alkyl, methyl and butyl (e.g., isobutyl). preferred examples of the heterocyclic ring structure are imidazopyridazine (more preferably 6-imidazo[1,2-*b*]pyridazine) and imidazolyl (more preferably 1-imidazolyl). For optional substitution of the cycloalkyl, aryl or heterocyclic ring, at least one (e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl) and nitro.

$R^{3'}$ represents -Z-M wherein Z represents O, S or NH and M represents H, an optionally substituted mono- or bi- cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, or an optionally substituted C_{5-10}aromatic ring structure (e.g., phenyl) optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or -Z-M -C(=O)NR^6R^7, -NR^6R^7, -OC(=O)NR^8R^9, -NC(=O)NR^8R^9 or -NC(=O)R^8;

Preferably, the heterocyclic ring structure is selected from imidazopyridazine (more preferably 6-imidazo[1,2-*b*]pyridazine) and imidazolyl (more preferably 1-imidazolyl). For optional substitution of the aromatic or heterocyclic ring structure, at least one (e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl) and nitro.

Most preferably, $R^{3'}$ is selected from -4-morpholinyl; -1-(2-methyl-5-nitro-imidazolyl); -1-(1,2,4-triazolyl); and -OC(=O)NH-Ph.

For R^4 and R^5, either:

(i) R^4 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; Z^2-(C_{1-8}alkyl)aryl, wherein Z^2 represents O or a bond, and the aryl is C_{6-10}, optionally substituted and optionally fused to a C_{5-10} heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted C_{6-10}aryl; an optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2 or 3 heteroatoms independently selected from O, N and S; (C_{1-8}alkyl)-R, wherein R represents an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted -C(=O)O(C_{1-8}alkyl); optionally substituted -C(=O)O-phenyl; optionally substituted -C(=O)(C_{1-8}alkyl); optionally substituted -C(=O)-phenyl; or -NHC(=O)R^6; and

R^5 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10} and optionally substituted; optionally substituted C_{6-10}aryl; or an optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or

(ii) the structure -NR^4R^5 represents a C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S and optionally fused to a C_{6-10}ring structure, -NR^4R^5 being optionally substituted.

For R^4 in option (i), preferably the C_{1-8}alkyl or the C_{1-8}alkyl in Z^2-(C_{1-8}alkyl)aryl or the C_{1-8}alkyl in (C_{1-8}alkyl)-R or the C_{1-8}alkyl in -C(=O)O(C_{1-8}alkyl) or the C_{1-8}alkyl in -C(=O)(C_{1-8}alkyl) is selected from C_{2-6}alkyl, methyl, ethyl, propyl (e.g., isopropyl), butyl (e.g., isobutyl or *tert*-butyl) and pentyl. Preferably, where C_{6-10}aryl is mentioned, the aryl is phenyl. Preferably, Z^2-(C_{1-8}alkyl)aryl represents Z^2-(C_{1-8}alkyl)benzodioxol. Preferably, for R^4, where a heterocyclic ring structure is mentioned, this is selected from furyl (e.g., 2-furyl), tetrahydrofuranyl (e.g., tetrahydro-2-furanyl), thienyl (e.g., 2-thienyl), morpholinyl (e.g., 4-morpholinyl), isoxazolyl (e.g., 4-isoxazolyl or 5-isoxazolyl), dioxoimidazolidinyl (e.g., 2,5-dioxoimidazolidinyl), pyrazinyl, dioxotetrahydropurinyl (e.g., 2,6-dioxo-1,2,3,6-tetrahydro-purin-7-yl), benzofuranyl (e.g., 2-benzofuranyl), pyridyl (e.g., 2-pyridyl or 3-pyridyl), quinolyl (e.g., 4-quinolyl), pyrrolidinyl (e.g., 2-pyrrolidinyl), piperazinyl (e.g., 1-piperazinyl), imidazopyridazinyl (e.g., imidazo[1,2-*b*]pyridazinyl) and tetrazolyl (e.g., tetrazol-2-yl, 1,2,3,4-tetrazol-2-yl). Preferably, for Z^2-(C_{1-8}alkyl)aryl, the aryl is optionally fused to a heterocyclic ring structure selected from furan, tetrahydrofuran, thiophene, morpholine, isoxazole, dioxoimidazolidine (e.g., 2,5-dioxoimidazolidine), pyrazine, dioxotetrahydropurine (e.g., 2,6-dioxo-1,2,3,6-tetrahydro-purine), benzofuran, pyridine, quinoline, pyrrolidine, piperazine, imidazopyridazine (e.g., imidazo[1,2-*b*]pyridazine) and tetrazole (e.g., 1,2,3,4-tetrazole). Preferably, the C_{3-8}cycloalkyl is selected from cyclopropyl C_{4-6}cycloalkyl and cyclopentyl. For optional substitution of the cycloalkyl, aryl, heterocycle or heterocyclic ring structure, at least one (e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl); phenyl; -O(C_{1-8}alkyl), preferably -O-methyl, -O-ethyl or -O(C_{3-6}alkyl); -C(=O)O(C_{1-8}alkyl), preferably -C(=O)O-methyl, -C(=O)O-ethyl or -C(=O)O(C_{3-6}alkyl); -C(=O)O-phenyl; -O-phenyl; -C(=O) (C_{1-8}alkyl), preferably -C(=O)-methyl, -C(=O)-ethyl or -C(=O)(C_{3-6}alkyl) ; -S(C_{1-8}alkyl), preferably -S-methyl, -S-ethyl or -S(C_{3-6}alkyl); OH; halogen (e.g., F, Cl or Br), NRR' where R and R' are independently H or C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl, most preferably R=R'=methyl); and nitro.

For option (ii), the C_{3-8}heterocyclic ring is preferably selected from piperidinyl (e.g., 1-piperidinyl), piperazinyl (e.g., 1-piperazinyl), morpholinyl (e.g., 4-morpholinyl) and tetrazolyl (e.g., 1,2,3,4-tetrazol-2-yl). Preferably, the C_{6-10} ring structure is selected from cyclohexyl and a benzo ring. For optional substitution of -NR^4R^5, at least one(e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl); phenyl; OCF_3; $OCHF_2$; -O(C_{1-8}alkyl), preferably -O-methyl, -O-

ethyl or -O(C_{3-6}alkyl); -C(=O)O(C_{1-8}alkyl), preferably -C(=O)O-methyl, -C(=O)O-ethyl, -C(=O)O-*tert*-butyl or -C(=O)O(C_{3-6}alkyl); -O-phenyl; -C(=O) (C_{1-8}alkyl), preferably -C(=O)-methyl, -C(=O)-ethyl or -C(=O)(C_{3-6}alkyl) ; -C(=O)OH; -S(C_{1-8}alkyl), preferably -S-methyl, -S-ethyl or -S(C_{3-6}alkyl); OH; halogen (e.g., F, Cl or Br), NRR' where R and R' are independently H or C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl, most preferably R=R'=methyl); and nitro.

For R^6 and R^7, either:

(i) R^6 is H; C_{1-12}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; optionally substituted (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10}; optionally substituted (C_{1-8}alkyl)R, where R represents a mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S or R represents a mono-, bi- or tri-cyclic C_{3-13}cycloalkyl; optionally substituted C_{6-10}aryl; an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; or -C(=O)-O-Ar, wherein Ar represents optionally substituted C_{6-10}aryl; and R^7 is H; or

(ii) the structure -NR^6R^7 represents a C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S and optionally fused to a C_{6-10}ring structure, -NR^6R^7 being optionally substituted.

For R^6 in option (ii), preferably C_{1-12}alkyl is selected from C_{1-8}alkyl, C_{2-6}alkyl, methyl, propyl (e.g., isopropyl), butyl (e.g., isobutyl or *tert*-butyl), pentyl and adamantyl (e.g., 1-adamantyl). For C_{1-8}alkyl in (C_{1-8}alkyl)aryl or (C_{1-8}alkyl)R, the alkyl is selected from C_{2-6}alkyl, methyl, propyl (e.g., isopropyl), butyl (e.g., isobutyl or *tert*-butyl) and pentyl. Preferably, where C_{6-10}aryl is mentioned, the aryl is phenyl. Preferably, Z^2-(C_{1-8}alkyl)aryl represents Z^2-(C_{1-8}alkyl)benzodioxol. Preferably, where a 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle is mentioned, this is selected from benzofuryl (e.g., benzofur-2-yl), furyl (e.g., 2-furyl), tetrahydrofuranyl (e.g., tetrahydro-2-furanyl), thienyl (e.g., 2-thienyl), morpholinyl (e.g., 4-morpholinyl), isoxazolyl (e.g., 4-isoxazolyl or 5-isoxazolyl), dioxoimidazolidinyl (e.g., 2,5-dioxoimidazolidinyl), pyrazinyl, dioxotetrahydropurinyl (e.g., 2,6-dioxo-1,2,3,6-tetrahydro-purin-7-yl), benzofuranyl (e.g., 2-benzofuranyl), pyridyl (e.g., 2-pyridyl or 3-pyridyl), quinolyl (e.g., 4-quinolyl), pyrrolidinyl (e.g., 2-pyrrolidinyl), piperazinyl (e.g., 1-piperazinyl), imidazopyridazinyl (e.g., imidazo[1,2-*b*]pyridazinyl) and tetrazolyl (e.g., tetrazol-2-yl, 1,2,3,4-tetrazol-2-yl). Preferably, the C_{3-8}cycloalkyl is selected from cyclopropyl C_{4-6}cycloalkyl and cyclopentyl. For optional substitution of the cycloalkyl, alkylaryl, aryl or

heterocycle, at least one (e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl); phenyl; OCF_3; $OCHF_2$; -O(C_{1-8}alkyl), preferably -O-methyl, -O-ethyl or -O(C_{3-6}alkyl); -C(=O)O(C_{1-8}alkyl), preferably -C(=O)O-methyl, -C(=O)O-ethyl, -C(=O)O-*tert*-butyl or -C(=O)O(C_{3-6}alkyl); -C(=O)O-phenyl; -O-phenyl; -C(=O) (C_{1-8}alkyl), preferably -C(=O)-methyl, -C(=O)-ethyl or -C(=O)(C_{3-6}alkyl) ; -C(=O)OH; -S(C_{1-8}alkyl), preferably -S-methyl, -S-ethyl or -S(C_{3-6}alkyl); OH; halogen (e.g., F, Cl or Br), NRR' where R and R' are independently H or C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl, most preferably R=R'=methyl); and nitro.

For option (ii), the C_{3-8}heterocyclic ring is preferably selected from piperidinyl (e.g., 1-piperidinyl), piperazinyl (e.g., 1-piperazinyl), morpholinyl (e.g., 4-morpholinyl) and tetrazolyl (e.g., 1,2,3,4-tetrazol-2-yl). Preferably, the C_{6-10}ring structure is selected from cyclohexyl and a benzo ring. For optional substitution of -NR^6R^7, at least one (e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl); phenyl; OCF_3; $OCHF_2$; -O(C_{1-8}alkyl), preferably -O-methyl, -O-ethyl or -O(C_{3-6}alkyl); -C(=O)O(C_{1-8}alkyl), preferably -C(=O)O-methyl, -C(=O)O-ethyl or -C(=O)O(C_{3-6}alkyl); -O-phenyl; -C(=O) (C_{1-8}alkyl), preferably -C(=O)-methyl, -C(=O)-ethyl or -C(=O)(C_{3-6}alkyl) ; -S(C_{1-8}alkyl), preferably -S-methyl, -S-ethyl or -S(C_{3-6}alkyl); OH; halogen (e.g., F, Cl or Br), NRR' where R and R' are independently H or C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl, most preferably R=R'=methyl); and nitro.

In formula I, a represents 1, 2, 3, 4 or 5 (preferably 1 or 2); each b independently represents 1, 2, 3, 4 or 5 (preferably 1 or 2); c represents 1, 2, 3, 4 or 5 (preferably 1 or 2); c' represents 1, 2, 3, 4 or 5 (preferably 1 or 2); d represents 1, 2, 3, 4 or 5 (preferably 1 or 2); each e independently represents 1, 2, 3, 4 or 5 (preferably 1 or 2); f represents 1, 2, 3, 4 or 5 (preferably 1 or 2); and g represents zero or represents 1, 2, 3, 4 or 5 (preferably 1 or 2).

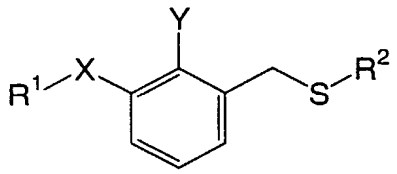
In the present specification, unless otherwise indicated, an alkyl substituent may be linear or branched.

Where optional substitution of aryl is mentioned, the substituent can be selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, and most preferably methyl); O(C_{3-8}cycloalkyl), preferably O-cyclopropyl, or O-cyclobutyl or O-cyclopentyl; O(C_{1-6}alkyl), preferably Omethyl or O(C_{2-4}alkyl); Hal, preferably Cl or F; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal, wherein Hal represents halogen (preferably F); NRR´, wherein R and R´ independently represent H or C_{1-8}alkyl (preferably methyl or C_{2-6}alkyl or C_{2-4}alkyl) , or NRR´ represents an optionally substituted C_{3-8}, preferably C_{3-6}, heterocyclic ring optionally

containing 1, 2 or 3 further heteroatoms independently selected from O, N and S; H; COOR″ or COR″, R″ representing H or C_{1-6}alkyl (preferably methyl, ethyl); or CH_2OH. For optional substitution of the heterocyclic ring represented by NRR´, at least one (e.g., one, two or three) substituents may be provided independently selected from C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl); phenyl; OCF_3; $OCHF_2$; -O(C_{1-8}alkyl), preferably -O-methyl, -O-ethyl or -O(C_{3-6}alkyl); -C(=O)O(C_{1-8}alkyl), preferably -C(=O)O-methyl, -C(=O)O-ethyl, -C(=O)O-*tert*-butyl or -C(=O)O(C_{3-6}alkyl); -C(=O)O-phenyl; -O-phenyl; -C(=O) (C_{1-8}alkyl), preferably -C(=O)-methyl, -C(=O)-ethyl or -C(=O)(C_{3-6}alkyl) ; -C(=O)OH; -S(C_{1-8}alkyl), preferably -S-methyl, -S-ethyl or -S(C_{3-6}alkyl); OH; halogen (e.g., F, Cl or Br), NRR' where R and R' are independently H or C_{1-6}alkyl (preferably C_{2-4}alkyl, more preferably methyl, most preferably R=R'=methyl); and nitro.

In one embodiment, a is 1, 2 or 3; b is 2; c' is 1, 2, 3, 4 or 5; d is 1, 2 or 3; e is 2; f is 1, 2 or 3; and g is 1 or 2.

Another embodiment has the general structure Ib



Ib

wherein:

X is S, S(=O), $S(=O)_2$ or O.

Y is C_{1-6}alkyl, O(C_{1-6}alkyl), Hal; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal.

R^1 is $-(CH_2)_a-R^3$, $-((CH_2)_2O)_c-R^3$, $-(CH_2)_d-R^{3'}$, $-(CH_2)_aC(=O)R^3$, $-(CH_2)_dC(=O)R^{3'}$, $-((CH_2)_2O)_{c'}-(CH_2)_f-R^{3'}$.

R^3 is C_{1-6}alkyl; optionally substituted C_{3-8}cycloalkyl optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or an optionally substituted 5- to 10-membered mono- or bi-cyclic heterocyclic ring structure containing 1, 2, 3, 4 or 5 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle.

$R^{3'}$ is -Z-M wherein Z represents O, S or NH and M represents H, an optionally substituted mono- or bi- cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure

containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; or an optionally substituted C_{5-10} aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or -Z-M represents $-C(=O)NR^6R^7$, $-NR^6R^7$, $-OC(=O)NR^8R^9$, $-NC(=O)NR^8R^9$ or $-NC(=O)R^8$.

For R^6 and R^7, either:

(i) R^6 is H; C_{1-12}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; optionally substituted (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10}; optionally substituted (C_{1-8}alkyl)R, where R represents a mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; or R represents a mono-, bi- or tri-cyclic C_{3-13}cycloalkyl; optionally substituted C_{6-10}aryl; an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; or -C(=O)-O-Ar, wherein Ar represents optionally substituted C_{6-10}aryl; and

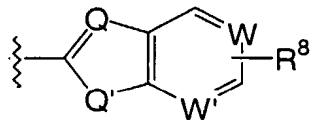
R^7 is H; or

(ii) the structure $-NR^6R^7$ represents a C_{3-8} heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; $-NR^6R^7$ being optionally substituted.

In one variation of the above embodiments, X is S or O; R^1 is $-(CH_2)_2R^3$, $-(CH_2)_2R^{3'}$, $-CH_2C(=O)R^3$ or $-CH_2C(=O)R^{3'}$; and R^3 is optionally substituted C_{3-8}cycloalkyl optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or an optionally substituted 5- to 10-membered mono- or bi-cyclic heterocyclic ring structure containing 1, 2, 3, 4 or 5 heteroatoms independently selected from O, N and S.

In another variation of the above embodiments, R^1 is selected from *-iso*-Bu, $-(CH_2CH_2O)_3CH_3$, $-(CH_2CH_2)$-4-morpholinyl, $-(CH_2CH_2O)_5CH_3$, $-(CH_2CH_2)$-1-(2-methyl-5-nitro-imidazolyl), $-(CH_2CH_2)$-1-(1,2,4-triazolyl), and $-(CH_2CH_2)$-OC(=O)NH-Ph.

In still another variation of the above embodiments, R^2 represents



wherein:

Q is CH or N;

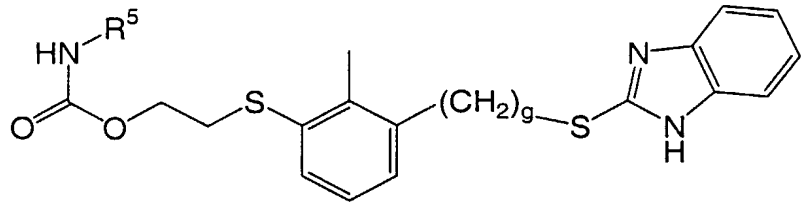
Q´ is NH, O or S;

W is CH or N;

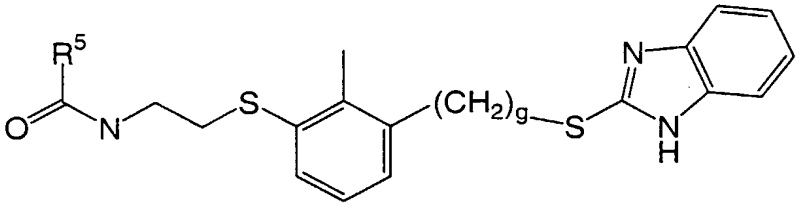
W´ is CH or N; and

R^8 is C_{1-6}alkyl; O(C_{3-8}cycloalkyl); O(C_{1-6}alkyl); Hal; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal, wherein Hal represents halogen; NRR´, wherein R and R´ independently represent H or C_{1-8}alkyl, or NRR´ represents an optionally substituted C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S; H; $COOR^9$ or COR^9, R^9 representing H or C_{1-6}alkyl; or CH_2OH.

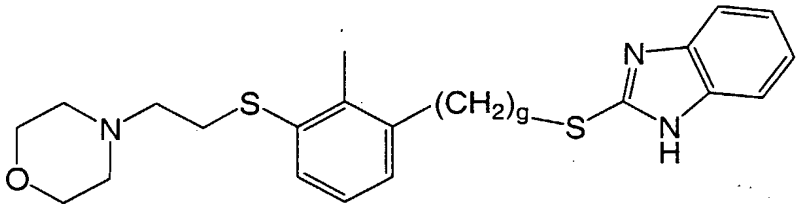
Preferred compounds are selected from compounds II, III, IV and V



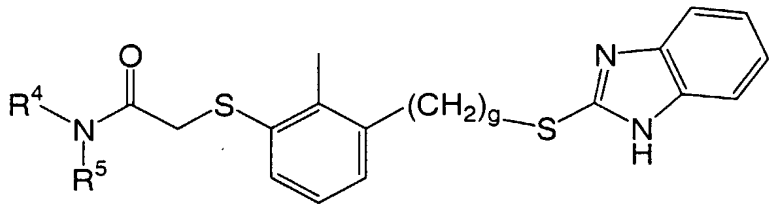
II



III



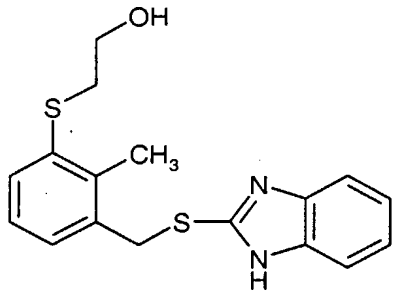
IV



V

Specific examples of compounds according to the invention are given below. Mass spectral molecular ion data are reported in units of m/z (mass/charge) in Daltons.

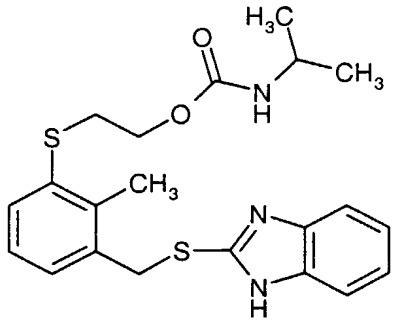
Compound 1



Mass spec' molecular ion: M+H= 331

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol

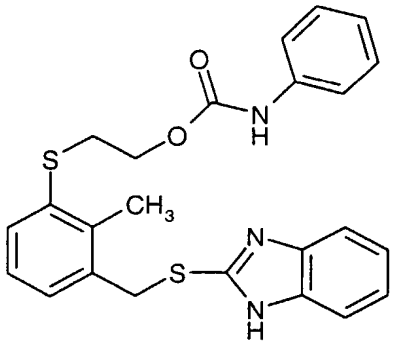
Compound 2



Mass spec' molecular ion: M+H=417

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl isopropylcarbamate

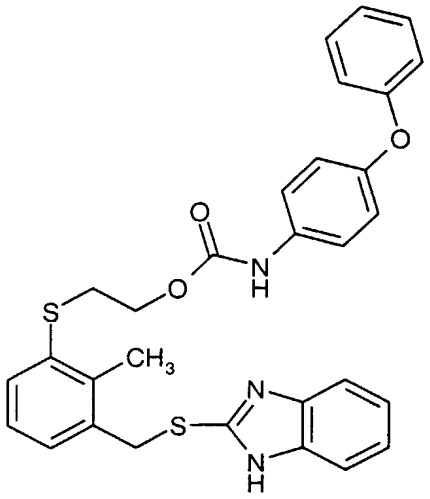
Compound 3



Mass spec' molecular ion: M+H= 450

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate

Compound 4

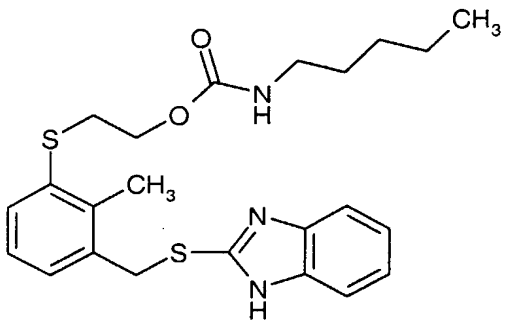


NMR:

^{1}H NMR (dmso-*d*6) ppm 2.42 (s, 3H), 3.26 (t, *J*=6.7 Hz, 2H), 4.22 (t, *J*=6.7 Hz, 2H), 4.62 (s, 2H), 6.95-7.68 (m, 16H), 9.57 (s, 1H, N*H*), 12.61 (s, 1H, N*H*).

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-phenoxyphenylcarbamate

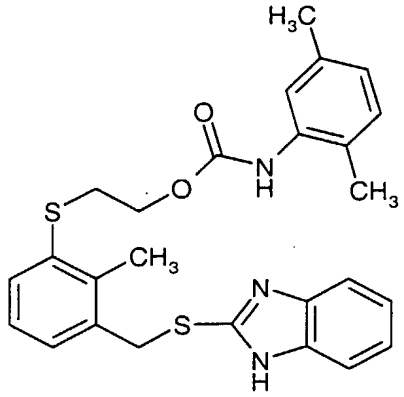
Compound 5



Mass spec' molecular ion: M+H= 445

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl pentylcarbamate

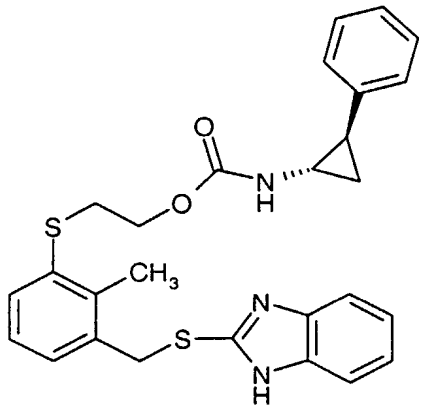
Compound 6



Mass spec' molecular ion: M+H= 479

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2,5-dimethylphenylcarbamate

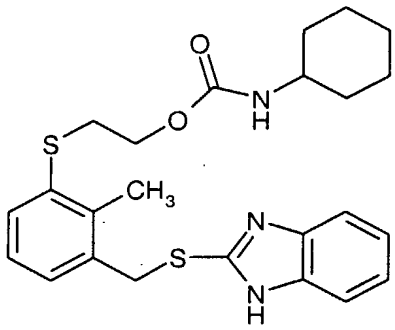
Compound 7



Mass spec' molecular ion: M+H= 490

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl (1*S*,2*R*)-2-phenylcyclopropylcarbamate

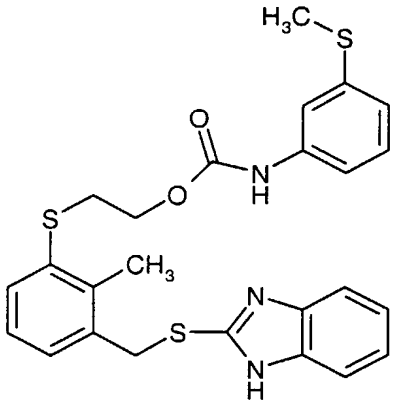
Compound 8



Mass spec' molecular ion: M+H= 456

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl cyclohexylcarbamate

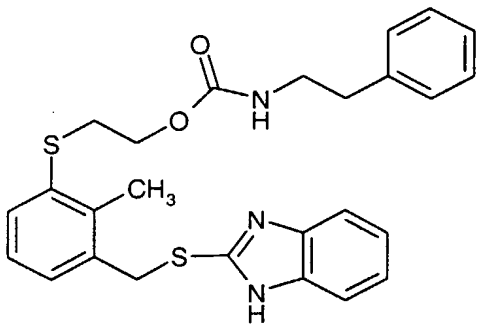
Compound 9



Mass spec' molecular ion: M+H= 496

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-(methylsulfanyl)phenylcarbamate

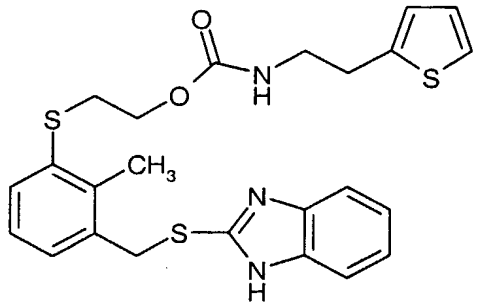
Compound 10



Mass spec' molecular ion: M+H= 478

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenethylcarbamate

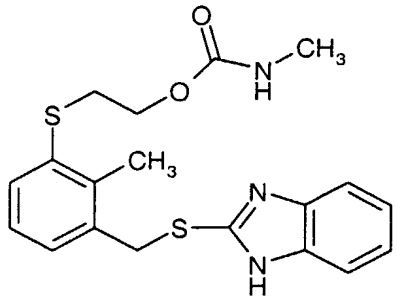
Compound 11



Mass spec' molecular ion: M+H= 484

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2-(2-thienyl)ethylcarbamate

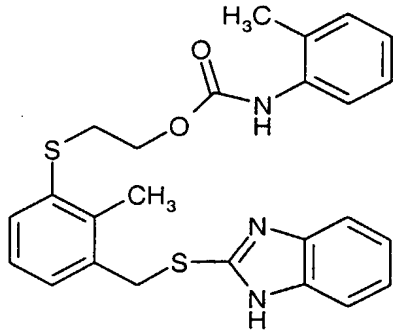
Compound 12



Mass spec' molecular ion: M+H= 388

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl methylcarbamate

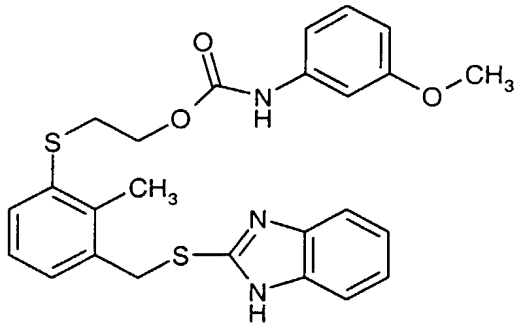
Compound 13



Mass spec' molecular ion: M+H= 464

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2-methylphenylcarbamate

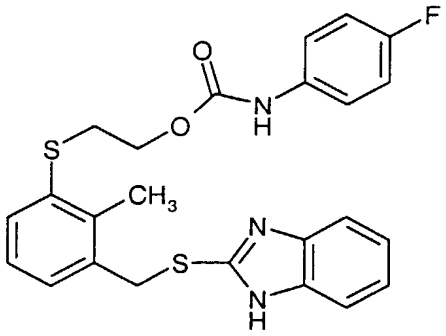
Compound 14



Mass spec' molecular ion: M+H= 480

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-methoxyphenylcarbamate

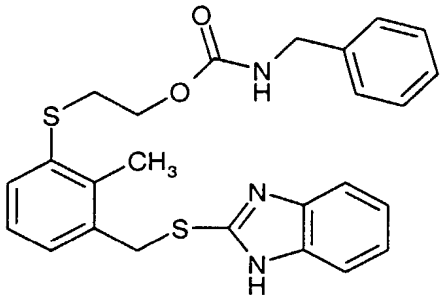
Compound 15



Mass spec' molecular ion: M+H= 468

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-fluorophenylcarbamate

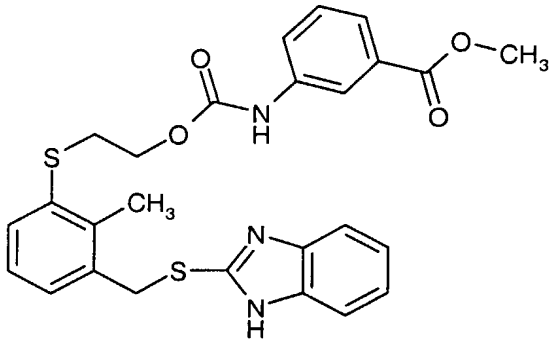
Compound 16



Mass spec' molecular ion: M+H= 464

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl benzylcarbamate

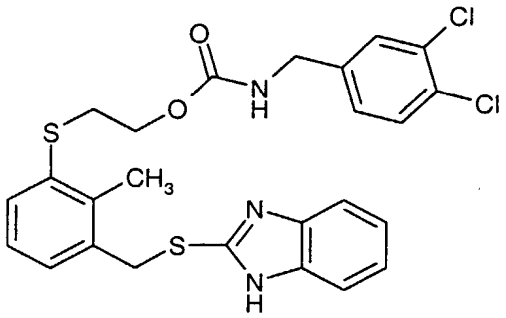
Compound 17



Mass spec' molecular ion: M+H= 508

methyl 3-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-ethoxy]carbonyl}amino)benzoate

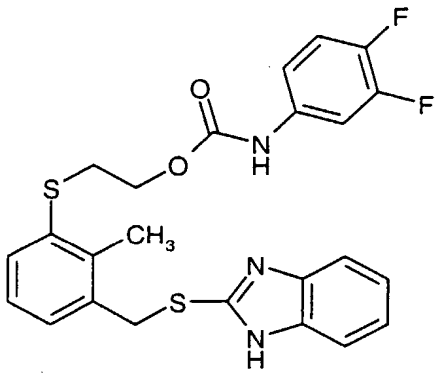
Compound 18



Mass spec' molecular ion: M+H= 532

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,4-dichlorobenzylcarbamate

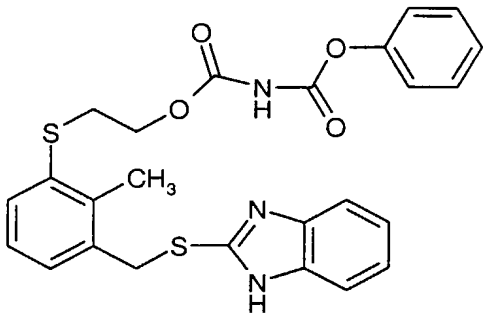
Compound 19



Mass spec' molecular ion: M+H= 486

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,4-difluorophenylcarbamate

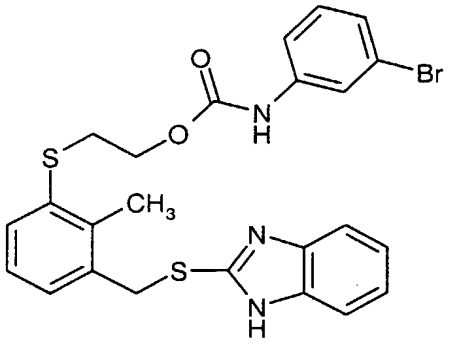
Compound 20



Mass spec' molecular ion: M+H= 494

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenyl dicarbonimidoate

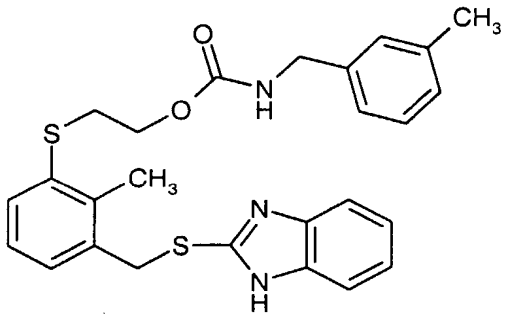
Compound 21



Mass spec' molecular ion: M+H= 529

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-bromophenylcarbamate

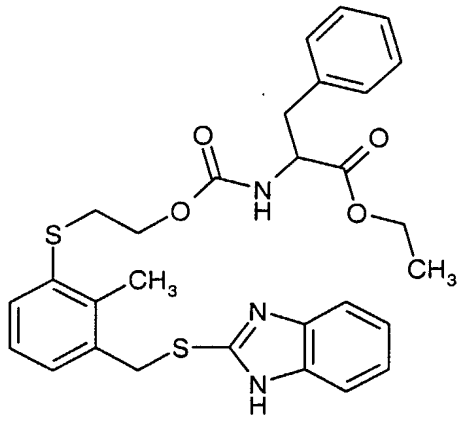
Compound 22



Mass spec' molecular ion: M+H= 478

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-methylbenzylcarbamate

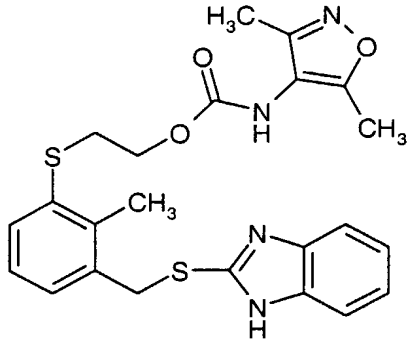
Compound 23



Mass spec' molecular ion: M+H= 550

ethyl 2-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]-carbonyl}amino)-3-phenylpropanoate

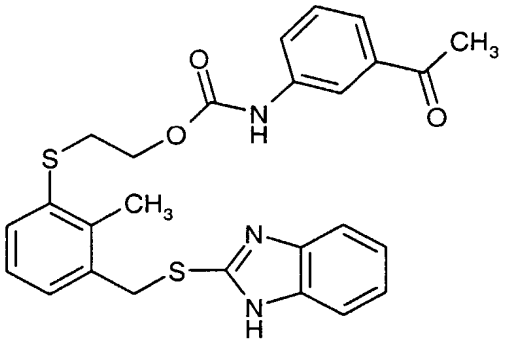
Compound 24



Mass spec' molecular ion: M+H= 469

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,5-dimethyl-4-isoxazolylcarbamate

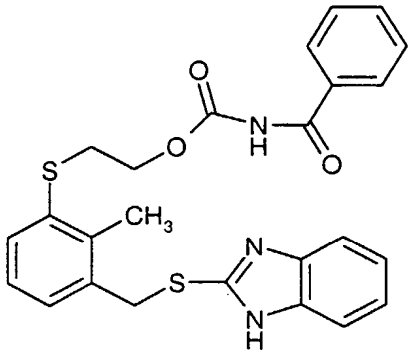
Compound 25



Mass spec' molecular ion: M+H= 492

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-acetylphenylcarbamate

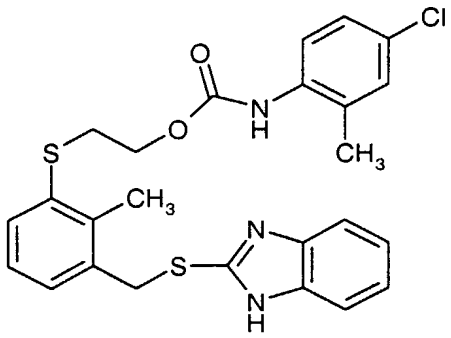
Compound 26



Mass spec' molecular ion: M+H= 478

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl benzoylcarbamate

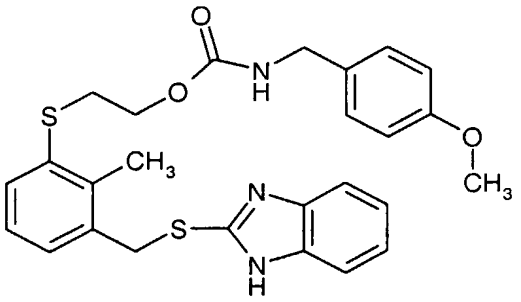
Compound 27



Mass spec' molecular ion: M+H= 499

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-chloro-2-methylphenylcarbamate

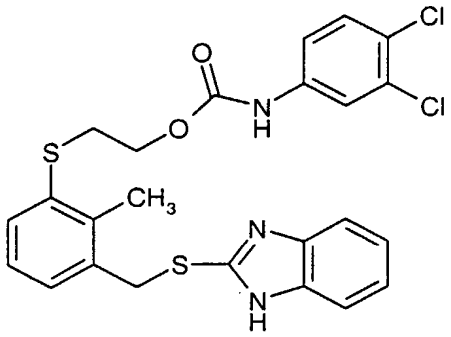
Compound 28



Mass spec' molecular ion: M+H= 494

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-methoxybenzylcarbamate

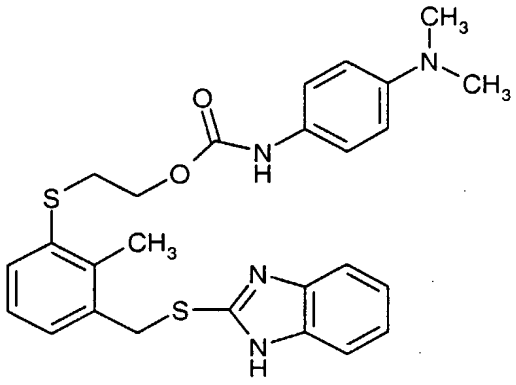
Compound 29



Mass spec' molecular ion: M+H= 518

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,4-dichlorophenylcarbamate

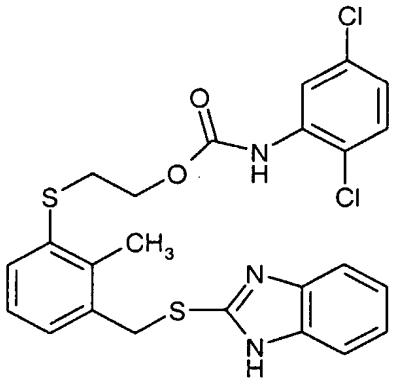
Compound 30



Mass spec' molecular ion: M+H= 493

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-(dimethylamino)phenylcarbamate

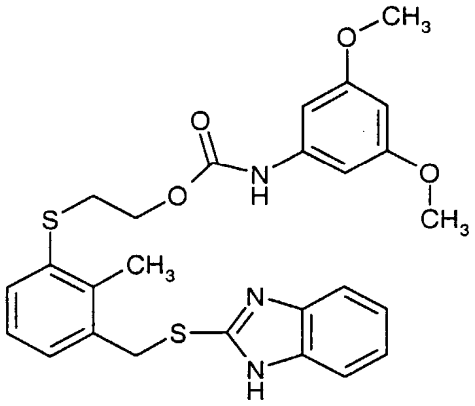
Compound 31



Mass spec' molecular ion: M+H= 518

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2,5-dichlorophenylcarbamate

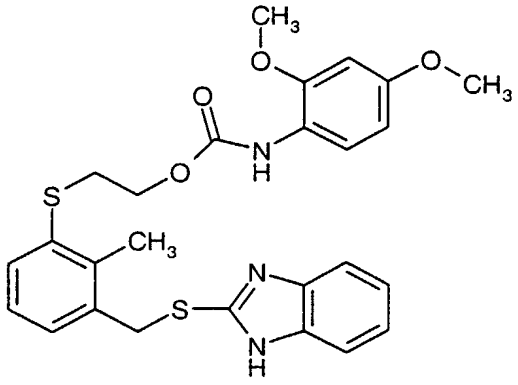
Compound 32



Mass spec' molecular ion: M+H= 510

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,5-dimethoxyphenylcarbamate

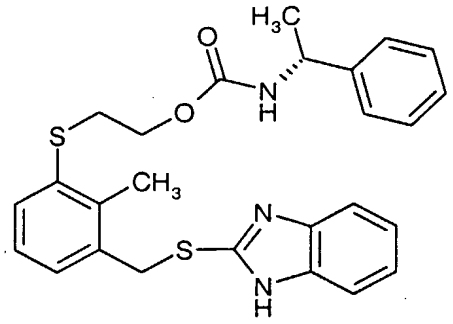
Compound 33



Mass spec' molecular ion: M+H= 510

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2,4-dimethoxyphenylcarbamate

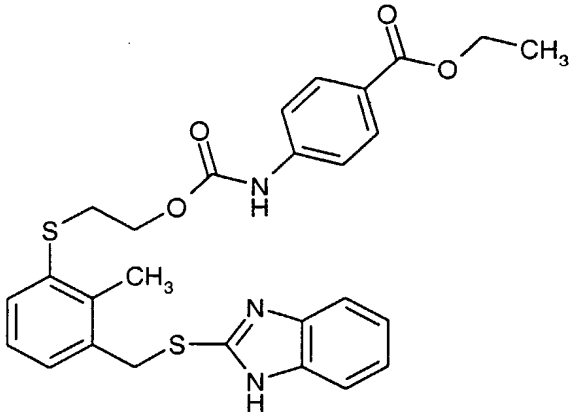
Compound 34



Mass spec' molecular ion: M+H= 478

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl (1*R*)-1-phenylethylcarbamate

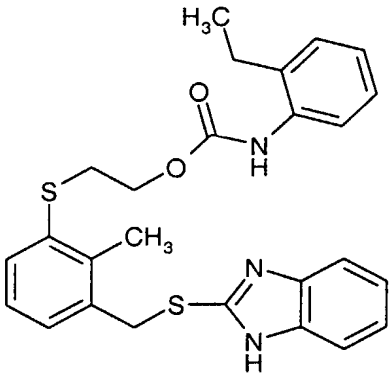
Compound 35



Mass spec' molecular ion: M+H= 522

ethyl 4-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}amino)benzoate

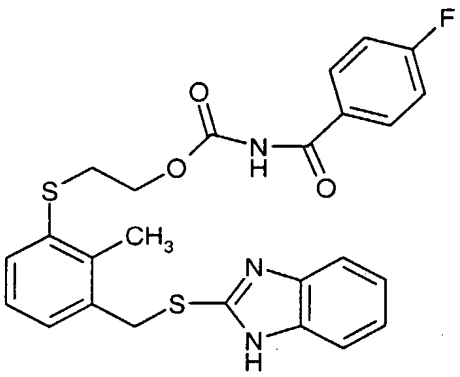
Compound 36



Mass spec' molecular ion: M+H= 478

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2-ethylphenylcarbamate

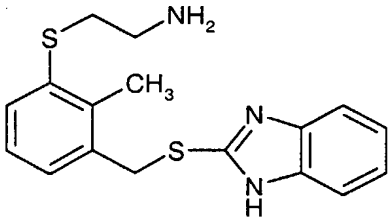
Compound 37



Mass spec' molecular ion: M+H= 496

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-fluorobenzoylcarbamate

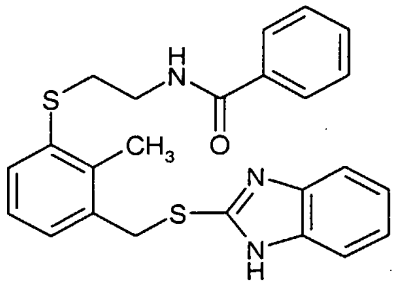
Compound 38



Mass spec' molecular ion: M+H= 330

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethylamine

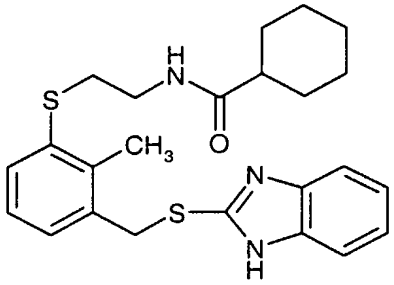
Compound 39



Mass spec' molecular ion: M+H= 434

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]benzamide

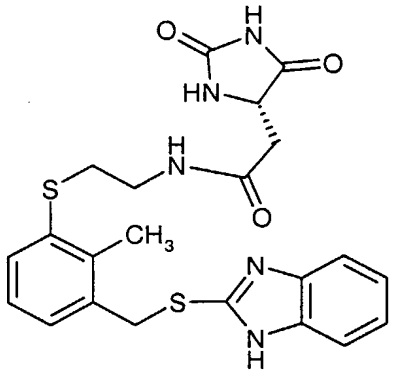
Compound 40



Mass spec' molecular ion: M+H= 440

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]cyclohexanecarboxamide

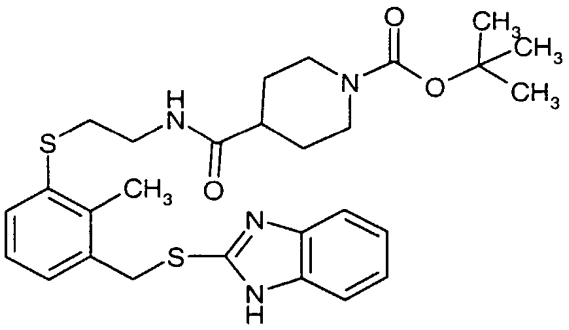
Compound 41



Mass spec' molecular ion: M+H= 470

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-[(4*S*)-2,5-dioxoimidazolidinyl]acetamide

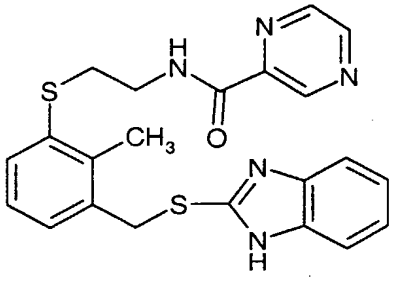
Compound 42



Mass spec' molecular ion: M+H= 541

tert-butyl 4-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]amino}carbonyl)-1-piperidinecarboxylate

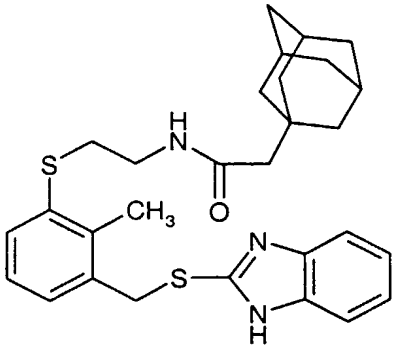
Compound 43



Mass spec' molecular ion: M+H= 436

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-pyrazinecarboxamide

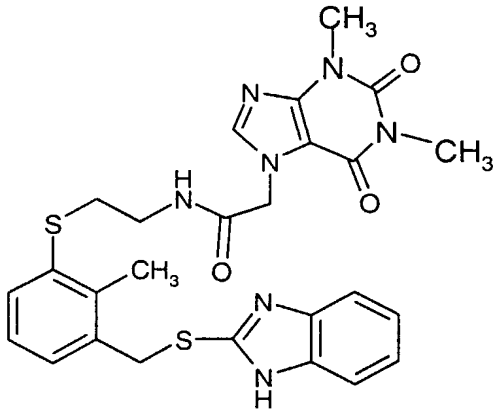
Compound 44



Mass spec' molecular ion: M+H= 506

2-(1-adamantyl)-*N*-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]acetamide

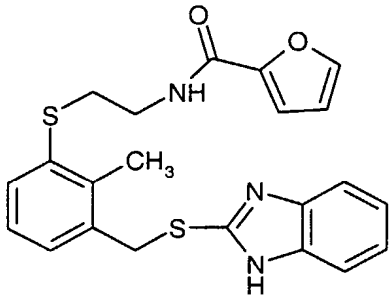
Compound 45



Mass spec' molecular ion: M+H= 550

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7*H*-purin-7-yl)acetamide

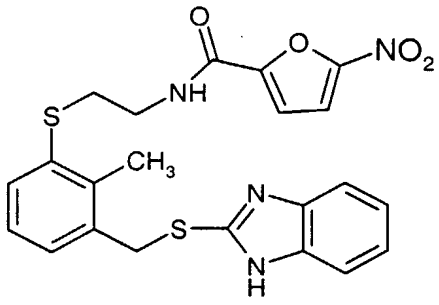
Compound 46



Mass spec' molecular ion: M+H= 424

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-furamide

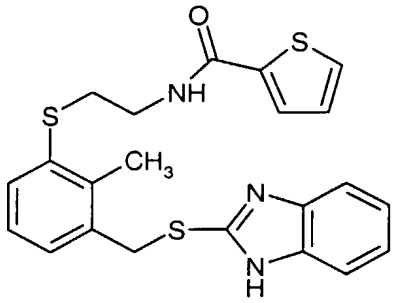
Compound 47



Mass spec' molecular ion: M+H= 469

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-5-nitro-2-furamide

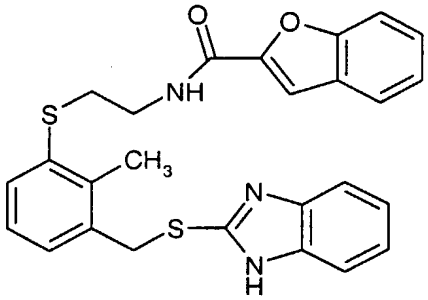
Compound 48



Mass spec' molecular ion: M+H= 440

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-thiophenecarboxamide

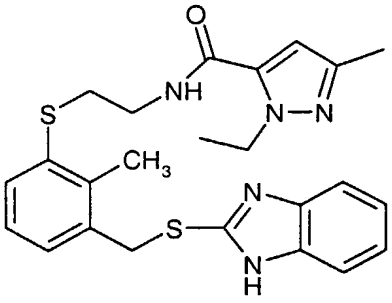
Compound 49



Mass spec' molecular ion: M+H= 474

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-1-benzofuran-2-carboxamide

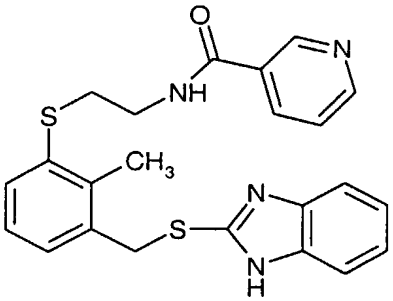
Compound 50



Mass spec' molecular ion: M+H= 466

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-1-ethyl-3-methyl-1*H*-pyrazole-5-carboxamide

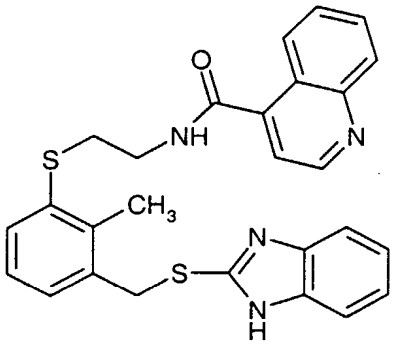
Compound 51



Mass spec' molecular ion: M+H= 435

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]nicotinamide

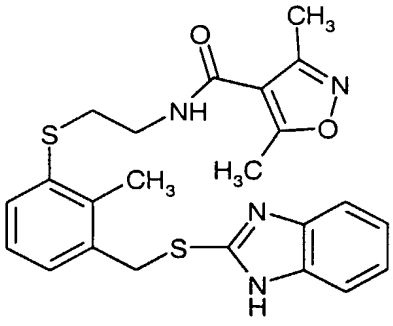
Compound 52



Mass spec' molecular ion: M+H= 485

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-4-quinolinecarboxamide

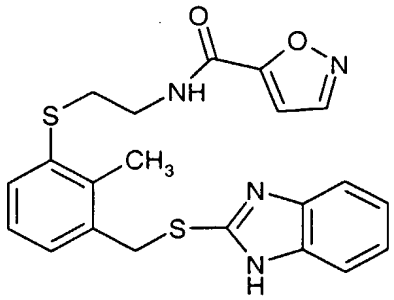
Compound 53



Mass spec' molecular ion: M+H= 453

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-3,5-dimethyl-4-isoxazolecarboxamide

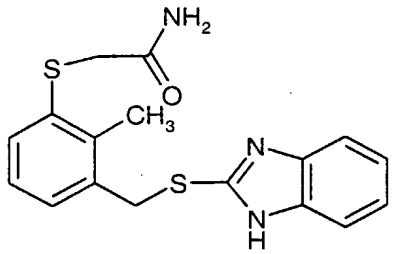
Compound 54



Mass spec' molecular ion: M+H= 425

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-5-isoxazolecarboxamide

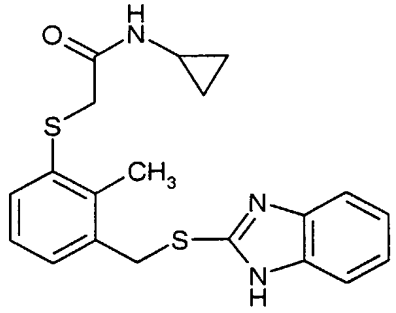
Compound 55



Mass spec' molecular ion: M+H= 344

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetamide

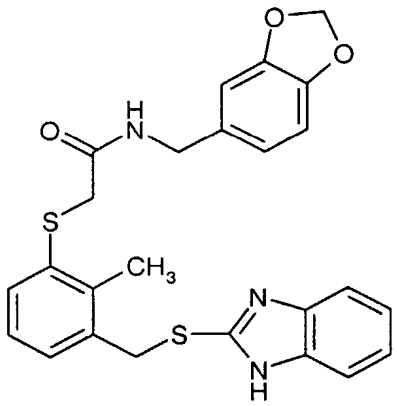
Compound 56



Mass spec' molecular ion: M+H= 384

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-cyclopropylacetamide

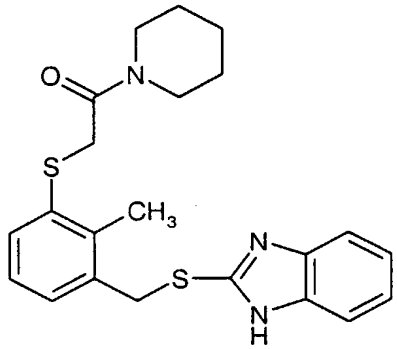
Compound 57



Mass spec' molecular ion: M+H= 478

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(1,3-benzodioxol-5-ylmethyl)acetamide

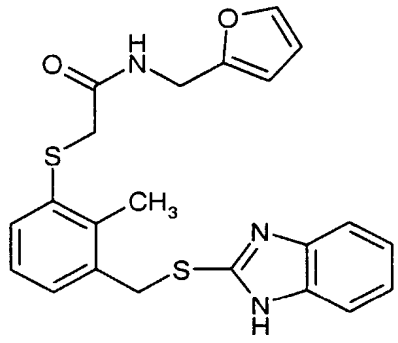
Compound 58



Mass spec' molecular ion: M+H= 412

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-(1-piperidinyl)-1-ethanone

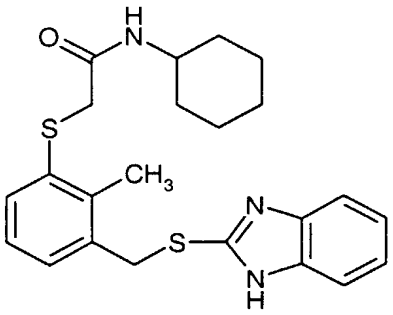
Compound 59



Mass spec' molecular ion: M+H= 424

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2-furylmethyl)acetamide

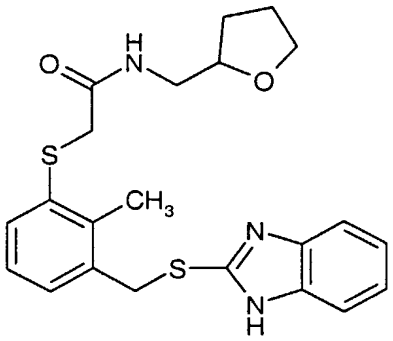
Compound 60



Mass spec' molecular ion: M+H= 426

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-cyclohexylacetamide

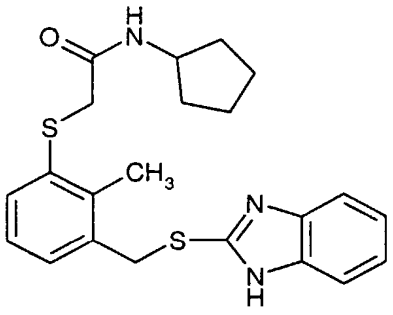
Compound 61



Mass spec' molecular ion: M+H= 428

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(tetrahydro-2-furanylmethyl)acetamide

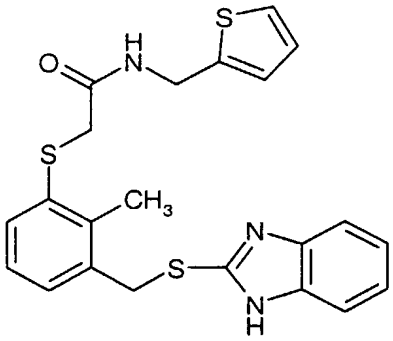
Compound 62



Mass spec' molecular ion: M+H= 412

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-cyclopentylacetamide

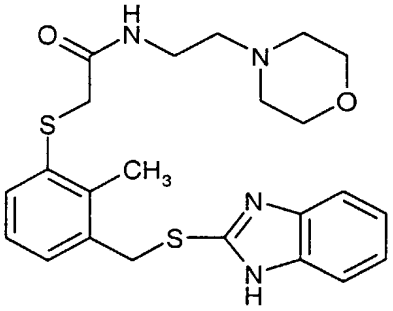
Compound 63



Mass spec' molecular ion: M+H= 440

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2-thienylmethyl)acetamide

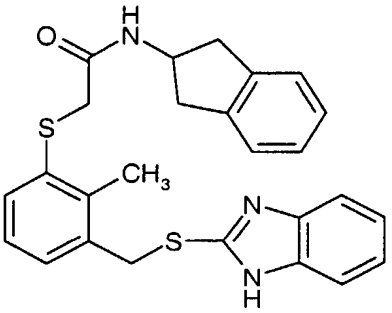
Compound 64



Mass spec' molecular ion: M+H= 457

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-[2-(4-morpholinyl)ethyl]acetamide

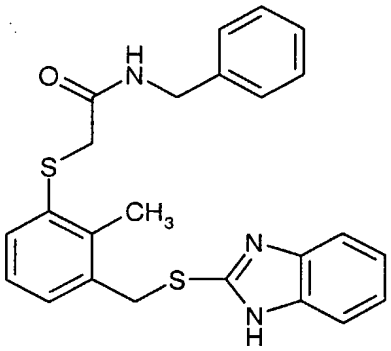
Compound 65



Mass spec' molecular ion: M+H= 460

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2,3-dihydro-1*H*-inden-2-yl)acetamide

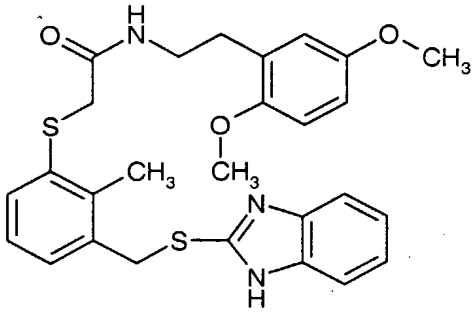
Compound 66



Mass spec' molecular ion: M+H= 434

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-benzylacetamide

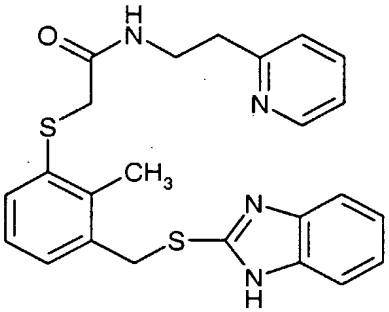
Compound 67



Mass spec' molecular ion: M+H= 508

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2,5-dimethoxyphenethyl)acetamide

Compound 68

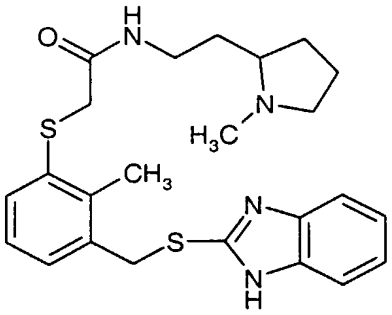


NMR:

^{1}H NMR (dmso-*d*6) ppm 2.42 (s, 3H), 2.71 (m, 2H), 3.77 (s, 2H), 4.37 (m, 2H), 4.62 (s, 2H), 7.10-7.16 (m, 7H), 7.56 (m, 1H), 7.66 (m, 1H), 8.49 (m, 1H), 8.75 (m, 1H), 12.61 (s, 1H, N*H*).

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-[2-(2-pyridinyl)ethyl]acetamide

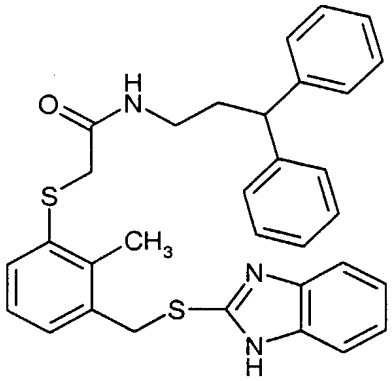
Compound 69



Mass spec' molecular ion: M+H= 455

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-[2-(1-methyl-2-pyrrolidinyl)ethyl]acetamide

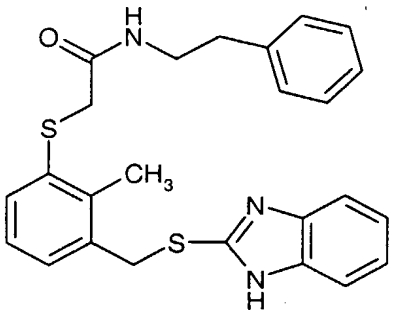
Compound 70



Mass spec' molecular ion: M+H= 538

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(3,3-diphenylpropyl)acetamide

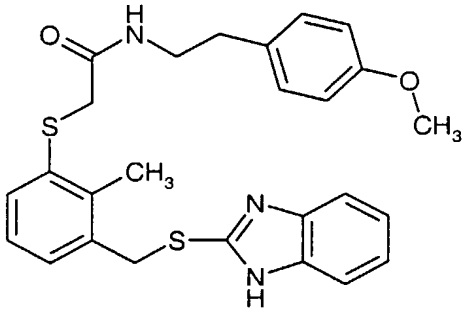
Compound 71



Mass spec' molecular ion: M+H= 449

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-phenethylacetamide

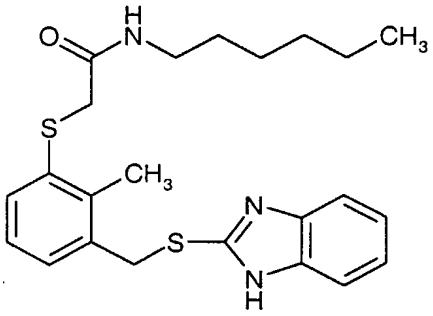
Compound 72



Mass spec' molecular ion: M+H= 479

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(4-methoxyphenethyl)acetamide

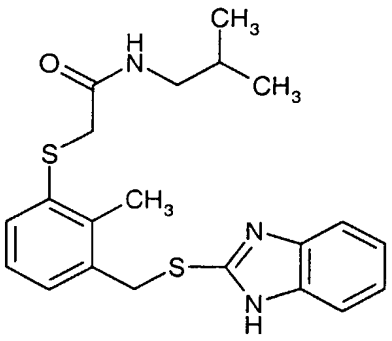
Compound 73



Mass spec' molecular ion: M+H= 429

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-hexylacetamide

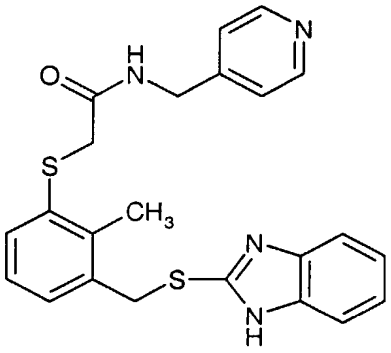
Compound 74



Mass spec' molecular ion: M+H= 401

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-isobutylacetamide

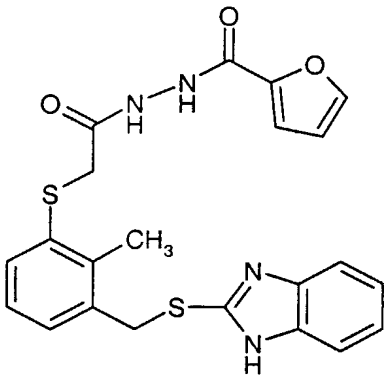
Compound 75



Mass spec' molecular ion: M+H= 436

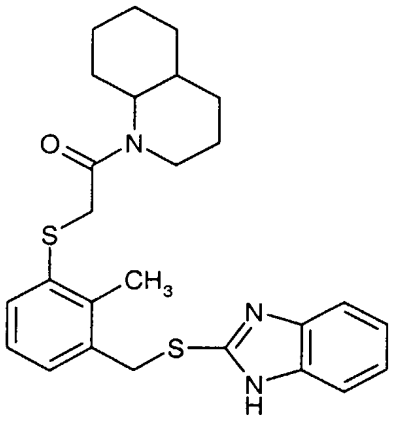
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(4-pyridinylmethyl)acetamide

Compound 76



N'-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetyl]-2-furohydrazide

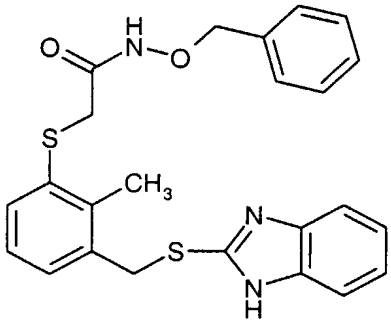
Compound 77



Mass spec' molecular ion: M+H= 467

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-octahydro-1(2*H*)-quinolinyl-1-ethanone

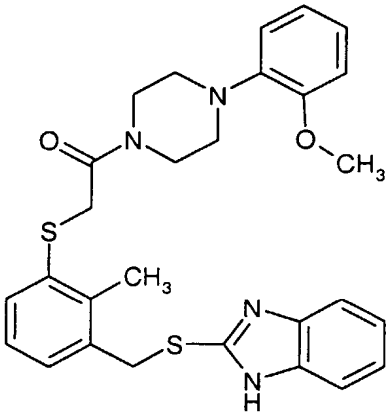
Compound 78



Mass spec' molecular ion: M+H= 450

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(benzyloxy)acetamide

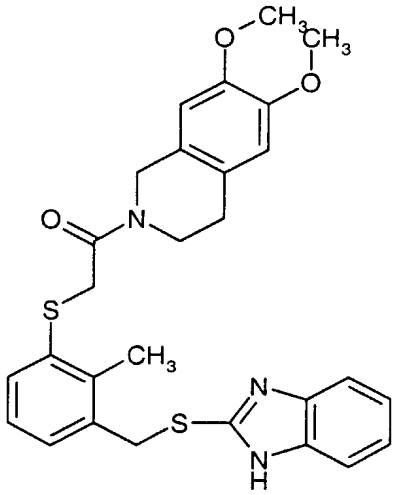
Compound 79



Mass spec' molecular ion: M+H= 519

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-[4-(2-methoxyphenyl)-1-piperazinyl]-1-ethanone

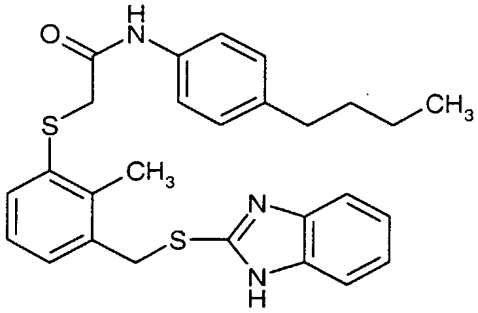
Compound 80



Mass spec' molecular ion: M+H= 521

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-[6,7-dimethoxy-3,4-dihydro-2(1*H*)-isoquinolinyl]-1-ethanone

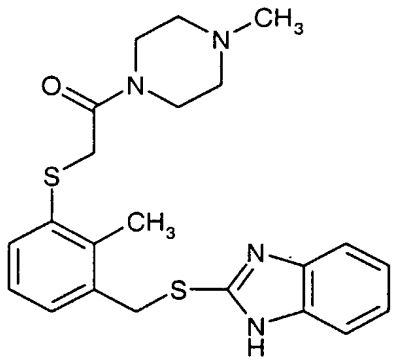
Compound 81



Mass spec' molecular ion: M+H= 477

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(4-butylphenyl)acetamide

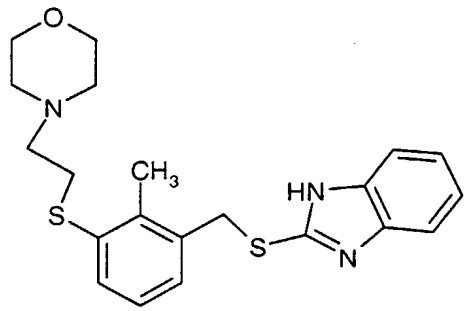
Compound 82



Mass spec' molecular ion: M+H= 427

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-(4-methyl-1-piperazinyl)-1-ethanone

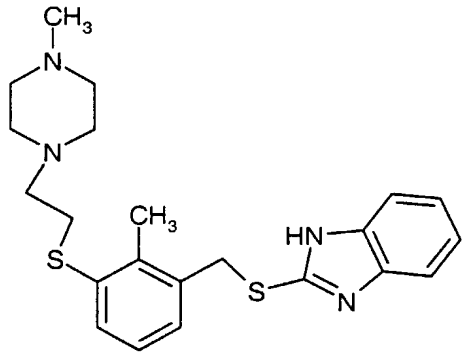
Compound 83



Mass spec' molecular ion: M+H= 400

2-[(2-methyl-3-{[2-(4-morpholinyl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole

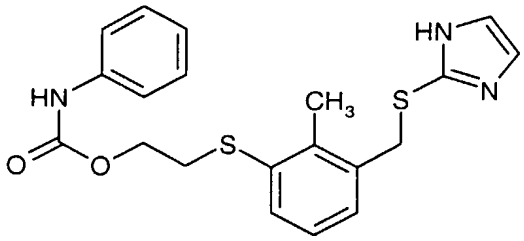
Compound 84



Mass spec' molecular ion: M+H= 413

2-[(2-methyl-3-{[2-(4-methyl-1-piperazinyl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole

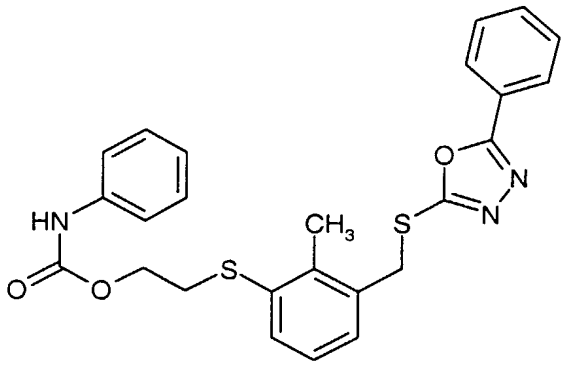
Compound 85



Mass spec' molecular ion: M+H= 400

2-({3-[(1*H*-imidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate

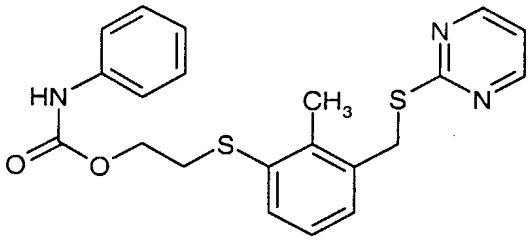
Compound 86



Mass spec' molecular ion: M+H= 478

2-[(2-methyl-3-{[(5-phenyl-1,3,4-oxadiazol-2-yl)sulfanyl]methyl}phenyl)sulfanyl]ethyl phenylcarbamate

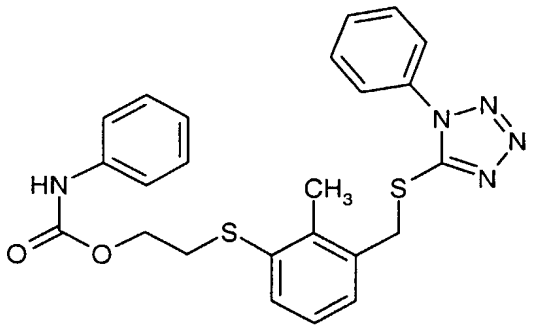
Compound 87



Mass spec' molecular ion: M+H= 412

2-({2-methyl-3-[(2-pyrimidinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate

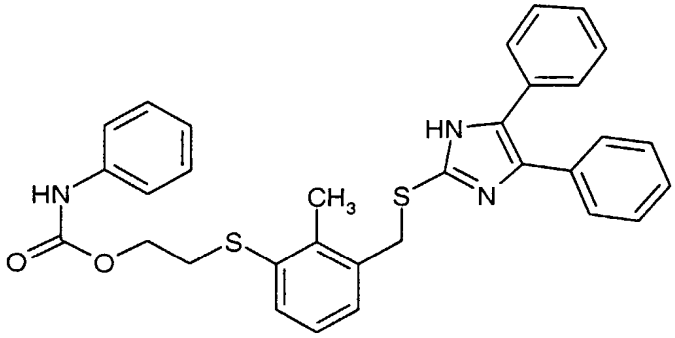
Compound 88



Mass spec' molecular ion: M+H= 478

2-[(2-methyl-3-{[(1-phenyl-1*H*-1,2,3,4-tetrazol-5-yl)sulfanyl]methyl}phenyl)sulfanyl]ethyl phenylcarbamate

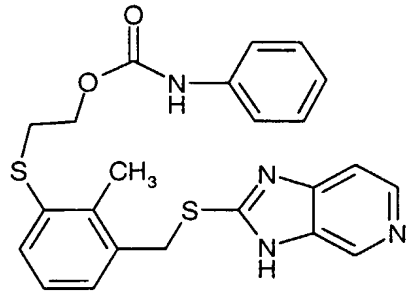
Compound 89



Mass spec' molecular ion: M+H= 552

2-[(3-{[(4,5-diphenyl-1*H*-imidazol-2-yl)sulfanyl]methyl}-2-methylphenyl)sulfanyl]ethyl phenylcarbamate

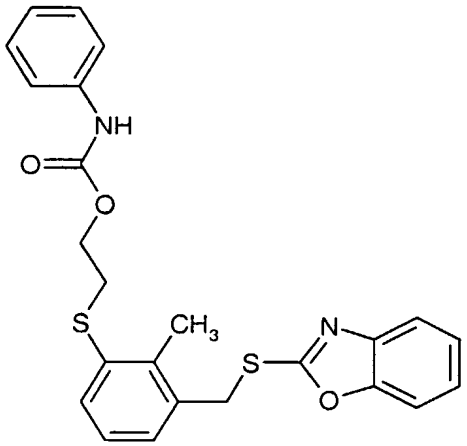
Compound 90



Mass spec' molecular ion: M+H= 451

2-({3-[(3*H*-imidazo[4,5-*c*]pyridin-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate

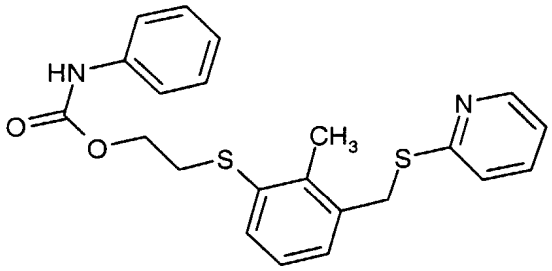
Compound 91



Mass spec' molecular ion: M+H= 451

2-({3-[(1,3-benzoxazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate

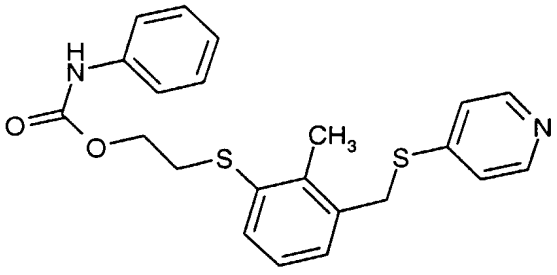
Compound 92



Mass spec' molecular ion: M+H= 411

2-({2-methyl-3-[(2-pyridinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate

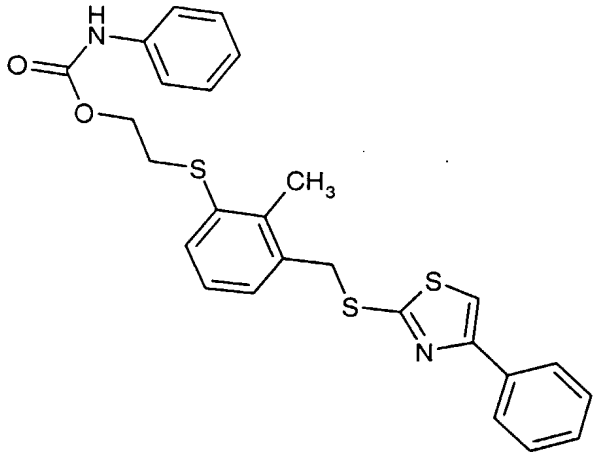
Compound 93



Mass spec' molecular ion: M+H= 411

2-({2-methyl-3-[(4-pyridinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate

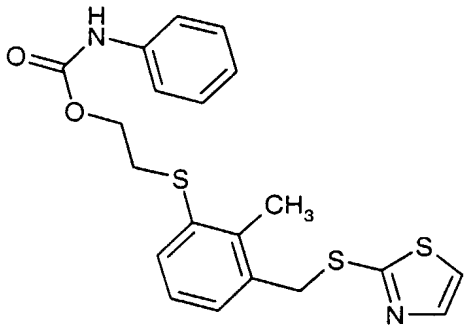
Compound 94



Mass spec' molecular ion: M+H= 493

2-[(2-methyl-3-{[(4-phenyl-1,3-thiazol-2-yl)sulfanyl]methyl}phenyl)sulfanyl]ethyl phenylcarbamate

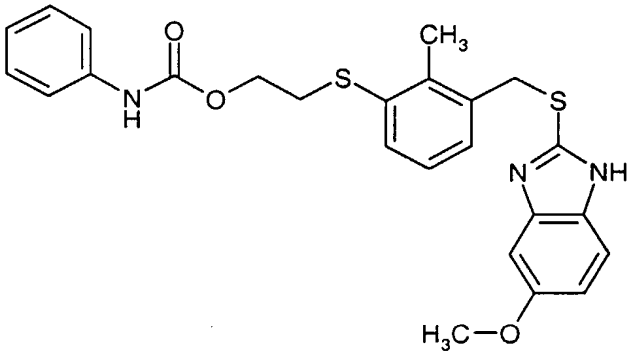
Compound 95



Mass spec' molecular ion: M+H= 417

2-({2-methyl-3-[(1,3-thiazol-2-ylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate

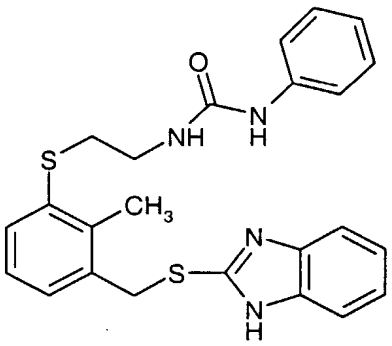
Compound 96



Mass spec' molecular ion: M+H= 480

2-[(3-{[(5-methoxy-1*H*-benzimidazol-2-yl)sulfanyl]methyl}-2-methylphenyl)sulfanyl]ethyl phenylcarbamate

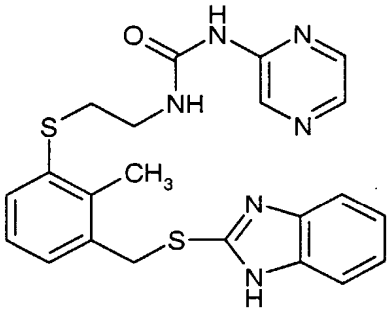
Compound 97



Mass spec' molecular ion: M+H= 449

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-*N'*-phenylurea

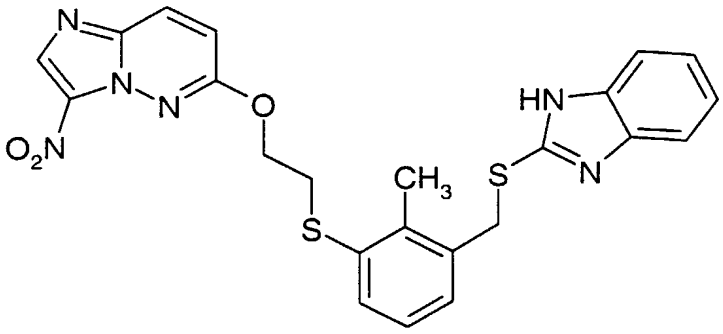
Compound 98



Mass spec' molecular ion: M+H= 451

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-*N'*-(2-pyrazinyl)urea

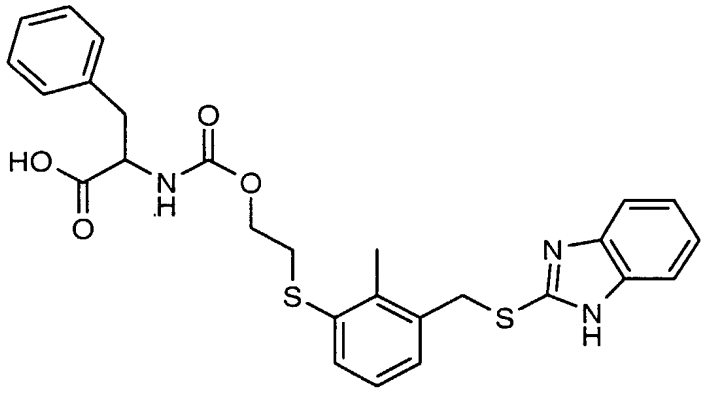
Compound 99



Mass spec' molecular ion: M+H= 493

6-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]-3-nitroimidazo[1,2-*b*]pyridazine

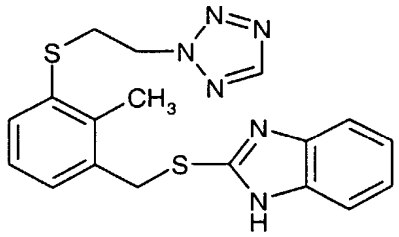
Compound 100



Mass spec' molecular ion: M+H= 522

N-{[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}phenylalanine

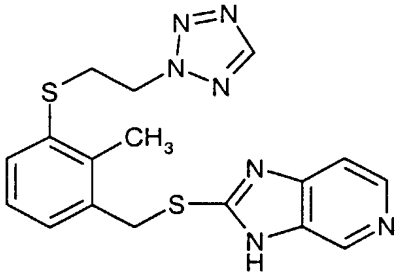
Compound 101



Mass spec' molecular ion: M+H= 383

2-[(2-methyl-3-{[2-(2*H*-1,2,3,4-tetrazol-2-yl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole

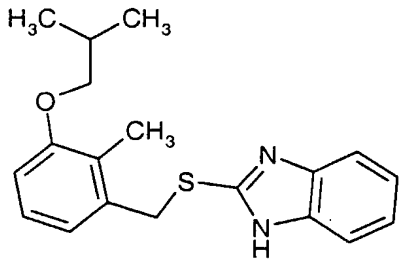
Compound 102



Mass spec' molecular ion: M+H= 384

2-[(2-methyl-3-{[2-(2*H*-1,2,3,4-tetrazol-2-yl)ethyl]sulfanyl}benzyl)sulfanyl]-3*H*-imidazo[4,5-*c*]pyridine

Compound 103

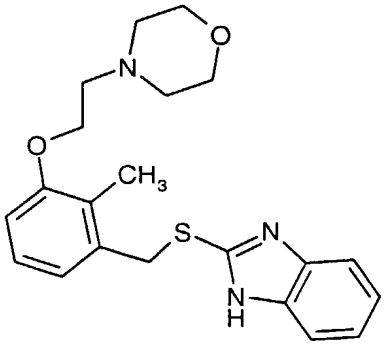


NMR:

400 MHz ^{1}H-NMR ($CHCl_3$-*d*) ppm 1.03 (d, 6H), 2.10 (m, 1H), 2.29 (s, 3H), 3.70 (d, 2H), 4.56 (s, 2H), 6.75 (d, 1H), 6.90 (d, 1H), 7.05 (t, 1H), 7.20 (t, 1H), 7.21 (t, 1H), 7.29 (d, 1H), 7.70 (d, 1H).

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1*H*-benzimidazole

Compound 104

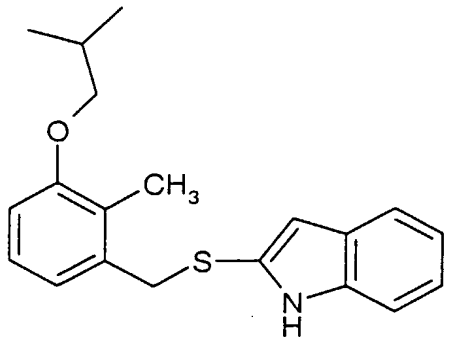


NMR:

500 MHz ^{1}H-NMR ($CHCl_3$-*d*) ppm 2.30 (s, 3H), 2.65 (m, 4H), 2.87 (m, 2H), 3.75 (m, 4H), 4.13 (m, 2H), 4.60 (s, 2H), 6.80 (d, 1H), 6.97 (d, 1H), 7.09 (t, 1H), 7.19-7.30 (m, 2H), 7.33 (d, 1H), 7.74 (d, 1H).

2-({2-methyl-3-[2-(4-morpholinyl)ethoxy]benzyl}sulfanyl)-1*H*-benzimidazole

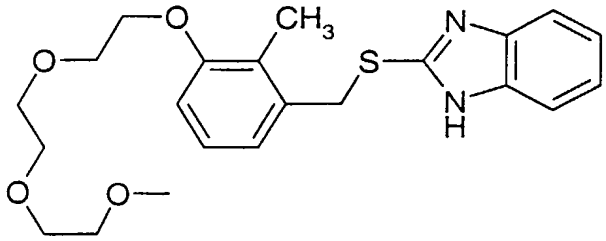
Compound 105



Mass spec' molecular ion: [M-H]= 324

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1*H*-indole

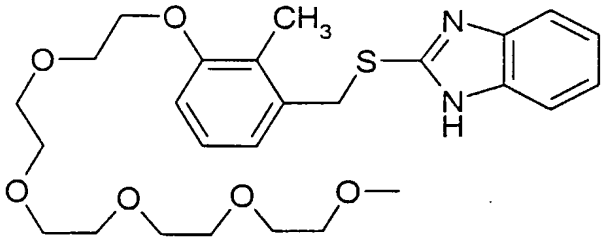
Compound 106



Mass spec' molecular ion: M+Na= 439

2-[(3-{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}-2-methylbenzyl)sulfanyl]-1*H*-benzimidazole

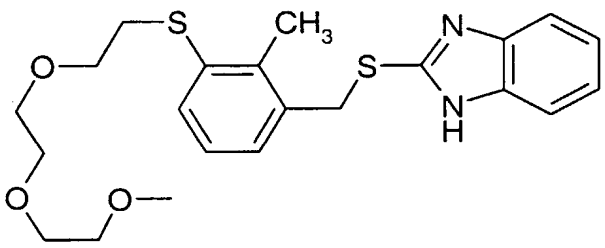
Compound 107



Mass spec' molecular ion: M+Na = 527

2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-yloxy)benzyl]sulfanyl}-1*H*-benzimidazole

Compound 108

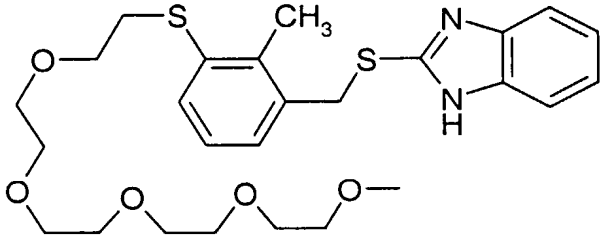


NMR:

500 MHz ^{1}H-NMR ($CHCl_3$-*d*) ppm 2.43 (s, 3H), 3.02 (t, 2H), 3.35 (s, 3H), 3.52-3.55 (m, 2H), 3.56-3.68 (m, 8H), 4.55 (s, 2H), 7.01 (t, 1H), 7.12 (d, 1H), 7.19-7.23 (m, 2H), 7.25 (d, 1H), 7.50-7.55 (m, 2H).

2-{[3-({2-[2-(2-methoxyethoxy)ethoxy]ethyl}sulfanyl)-2-methylbenzyl]sulfanyl}-1*H*-benzimidazole

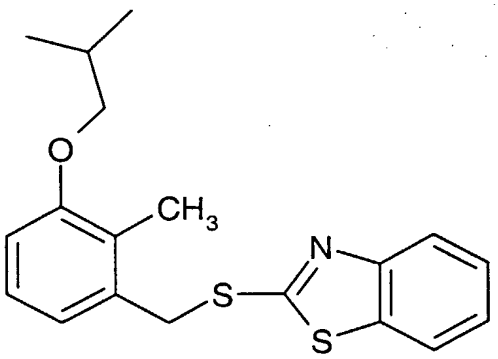
Compound 109



Mass spec' molecular ion: M+Na= 543

2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazole

Compound 110

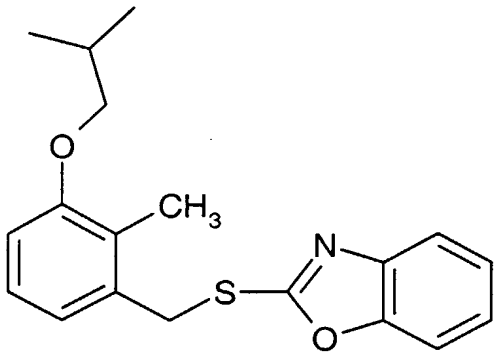


NMR:

600 MHz ^{1}H-NMR ($CHCl_3$-*d*) ppm 1.05 (d, 3H), 1.06 (d, 3H), 2.15 (m, 1H), 2.34 (s, 3H), 3.73 (d, 2H), 4.65 (s, 2H), 6.79 (d, 1H), 7.02 (d, 1H), 7.11 (t, 1H), 7.31 (t, 1H), 7.44 (t, 1H), 7.77 (d, 1H), 7.92 (d, 1H).

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1,3-benzothiazole

Compound 111

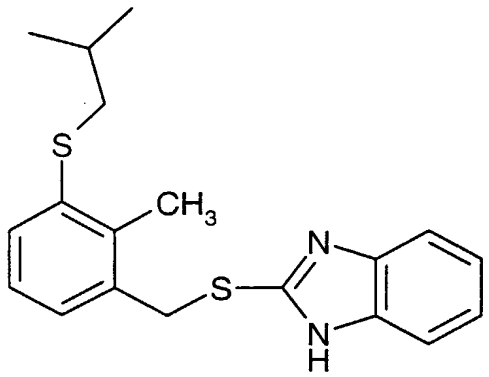


NMR:

600 MHz ^{1}H-NMR ($CHCl_3$-*d*) ppm 1.10 (d, 6H), 2.16 (m, 1H), 2.39 (s, 3H), 3.76 (d, 2H), 4.66 (s, 2H), 6.83 (d, 1H), 7.07 (d, 1H), 7.15 (t, 1H), 7.28 (t, 1H), 7.32 (t, 1H), 7.47 (d, 1H), 7.68 (d, 1H).

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1,3-benzoxazole

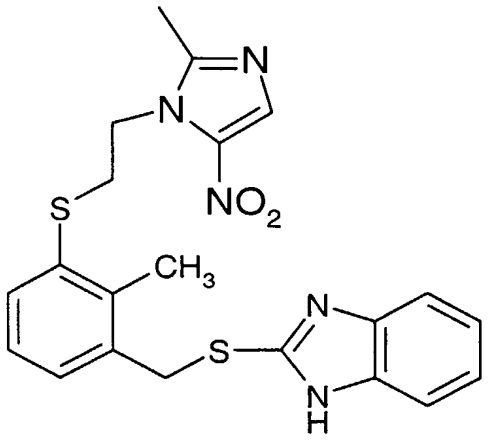
Compound 112



Mass spec' molecular ion: M+H= 343

2-{[3-(isobutylsulfanyl)-2-methylbenzyl]sulfanyl}-1*H*-benzimidazole

Compound 113

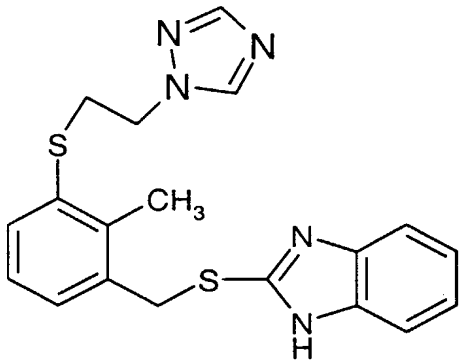


NMR:

300 MHz ^{1}H-NMR (CH_3OH-*d*4) ppm 2.26 (s, 3H), 2.43 (s, 3H), 3.29 (t, 2H), 4.40 (t, 2H), 4.49 (s, 2H), 4.89 (broad, >3H, exchangeable with D_2O), 7.02 (t, 1H), 7.09-7.19 (m, 3H), 7.29 (d, 1H), 7.36-7.49 (m, 2H), 7.79 (s, 1H).

2-[(2-methyl-3-{[2-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole

Compound 114

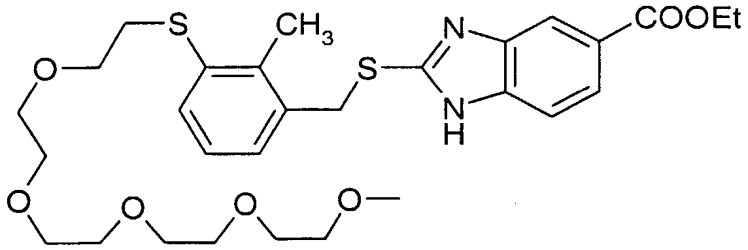


NMR:

300 MHz ^{1}H-NMR ($CHCl_3$-*d*) ppm 2.37 (s, 3H), 3.28 (t, 2H), 4.30 (t, 2H), 4.43 (s, 2H), 6.86-7.00 (m, 2H), 7.10-7.22 (m, 3H), 7.32-7.72 (broad, 2H), 7.87 (s, 1H), 7.91 (s, 1H).

2-[(2-methyl-3-{[2-(1*H*-1,2,4-triazol-1-yl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole

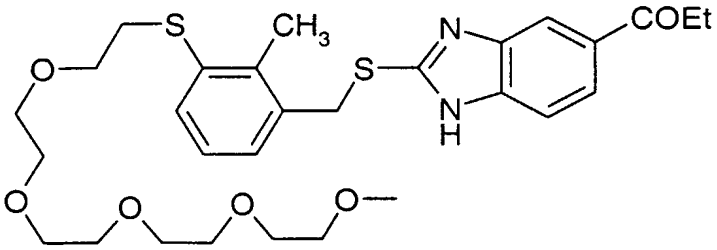
Compound 115



Mass spec' molecular ion: M+H= 593

ethyl 2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazole-5-carboxylate

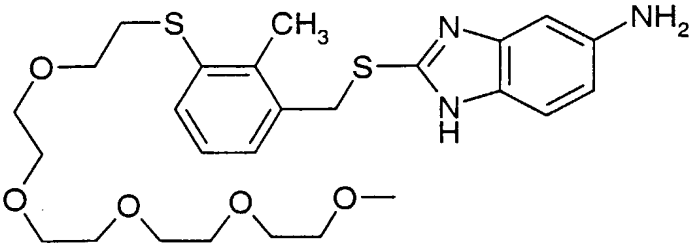
Compound 116



Mass spec' molecular ion: M+Na= 599

1-(2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazol-5-yl)-1-propanone

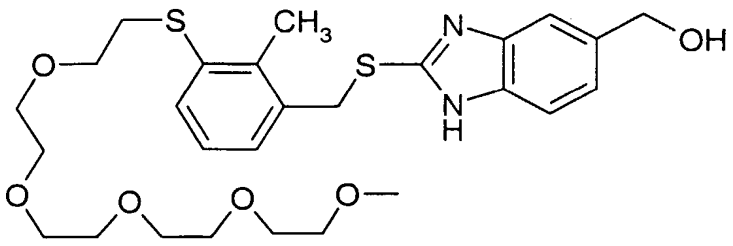
Compound 117



Mass spec' molecular ion: M+Na= 558

2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazol-5-amine

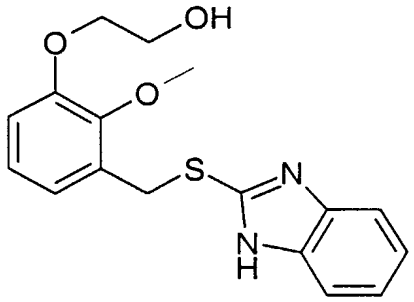
Compound 118



Mass spec' molecular ion: M+Na= 573

(2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazol-5-yl)methanol

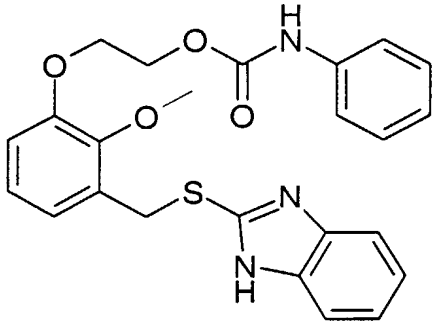
Compound 119



Mass spec' molecular ion: Mass spec' molecular ion: [M-H]- = 329

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methoxyphenoxy}-1-ethanol

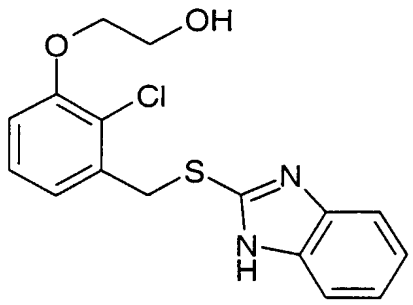
Compound 120



Mass spec' molecular ion: M+H= 450

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methoxyphenoxy}ethyl phenylcarbamate

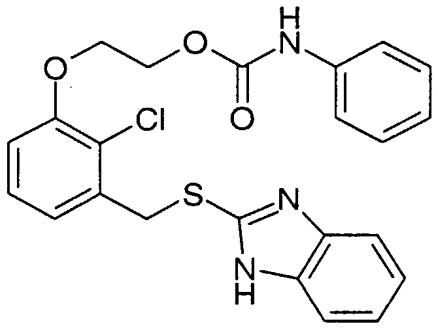
Compound 121



Mass spec' molecular ion: M+H= 335

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}-1-ethanol

Compound 122



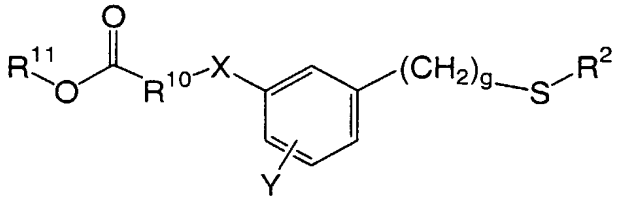
Mass spec' molecular ion: M+H= 454

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}ethyl phenylcarbamate

The compounds of formula I above may be converted to a pharmaceutically-acceptable salt or solvate thereof, preferably an acid addition salt such as a hydrochloride, hydrobromide, phosphate, acetate, fumarate, maleate, tartrate, citrate, oxalate, methanesulfonate or *p*-toluenesulfonate, or an alkali metal salt such as a sodium or potassium salt.

The compounds of formula I can be prepared by a process comprising any one of steps (a) to (h) as follows:

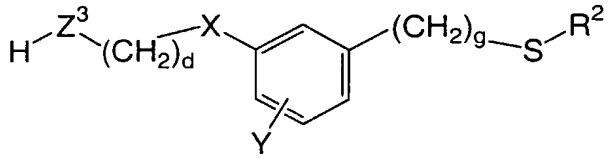
(a) reducing compound VI



VI

wherein R^{10} represents $(CH_2)_d$ or $-(CH_2)_{f-1}-O-(CH_2)_e-$ and R^{11} represents H or C_{1-6}alkyl; or

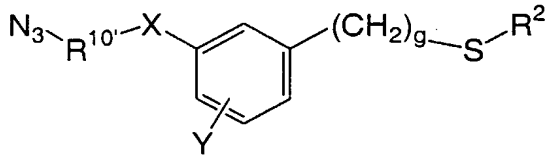
(b) reacting compound VII with R^6-NCO



VII

wherein Z^3 represents O or NH; or

(c) reducing compound VIII

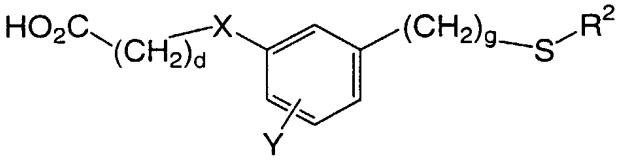


VIII

wherein $R^{10'}$ represents a bond, $(CH_2)_d$ or $-(CH_2)_f$-O-$(CH_2)_e$-; or

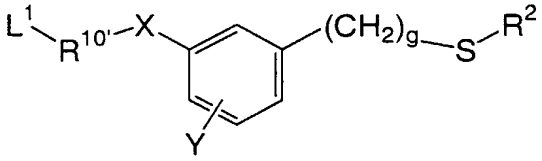
(d) reacting compound VII with R^6-COOH; or

(e) reacting compound IX with NHR^4R^5; or



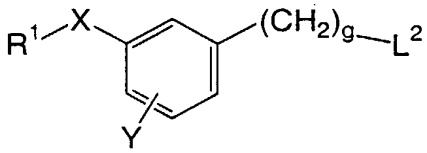
IX

(f) reacting compound X with NHR^4R^5



X

wherein L^1 represents a leaving group and $R^{10'}$ represents $(CH_2)_d$ or $-(CH_2)_f$-O-$(CH_2)_e$-; or

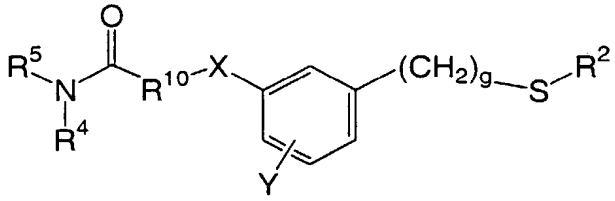


XI

(g) reacting compound XI with R^2-SH

wherein L^2 represents a leaving group; or

(h) reducing compound XII



XII

wherein R^{10} represents $(CH_2)_d$ or $-(CH_2)_{f-1}$-O-$(CH_2)_e$-.

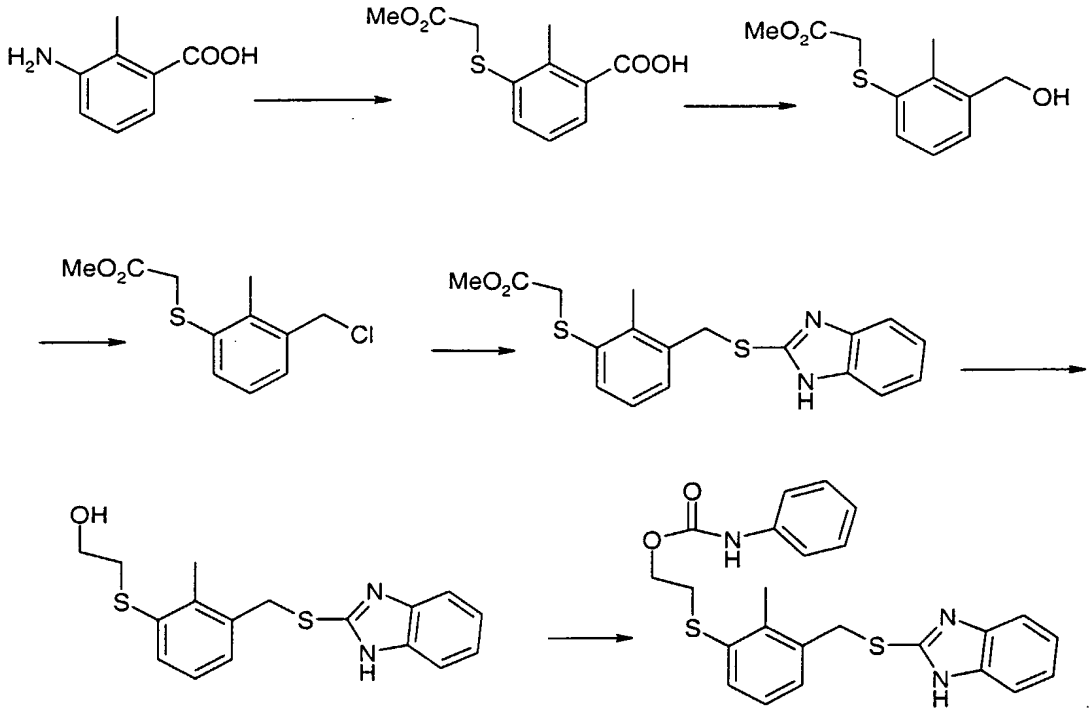
It will be appreciated by those skilled in the art that in the processes of the present invention certain functional groups such as hydroxyl or amino groups in the starting reagents or intermediate compounds may need to be protected by protecting groups. Thus, the preparation of the compounds of formula (I) may involve, at an appropriate stage, the addition and subsequent removal of one or more protecting groups.

The protection and deprotection of functional groups is described in 'Protective Groups in Organic Chemistry', edited by J.W.F. McOmie, Plenum Press (1973) and 'Protective Groups in Organic Synthesis', 2nd edition, T.W. Greene and P.G.M. Wuts, Wiley-Interscience (1991).

The compounds of the present invention have anti-*Helicobacter pylori* activity, i.e., they can be administered to a mammalian patient therapeutically to treat *Helicobacter pylori* infection in the patient and/or to prevent such infection. A further advantage of compounds of the invention is that they are particularly selective for *Helicobacter pylori*.

Experimental

Scheme 1



3-[(2-Methoxy-2-oxoethyl)sulfanyl]-2-methylbenzoic acid

3-amino-2-methylbenzoic acid, 11.3 g, was dissolved in H_2O (100 mL) and conc. HCL (15 mL) was added at 0 °C $NaNO_2$ (5.5 g) in H_2O (40 mL) was added to the above

suspension over 30min. The above diazonium salt was kept at 0°C and added slowly (over 40 min) to a solution of methyl thioglycolate, 8.48 g in 50 mL of MeOH at 60 °C. During the addition, the pH of the reaction medium was kept around 5 ~ 6 by adding sat. Na_2CO_3 very carefully. After the end of addition, the reaction was heated at 60 to 70 °C for additional 45min. The mixture was cooled to 0 °C and pH was adjusted to ~ 1 with conc. HCL & extracted with EtOAc, dried over Na_2SO_4, filtered, and the solvent was evaporated to give 17.4 g of crude 3-[(2-methoxy-2-oxoethyl)sulfanyl]-2-methylbenzoic acid.

Methyl 2-{[3-(hydroxymethyl)-2-methylphenyl]sulfanyl}acetate

3-[(2-methoxy-2-oxoethyl)sulfanyl]-2-methylbenzoic acid, 15.4 g, was dissolved in 120 mL THF and cooled on an ice bath. Borane-THF solution, 130 mL (1M in THF) was added slowly. The reaction was stirred for 1 hour then quenched with ice water, extracted with EtOAc, dried over Na_2SO_4, purified by flash chromatography (silica gel, CH_2Cl_2/EtOAc = 20/1) to give 5 grams of methyl 2-{[3-(hydroxymethyl)-2-methylphenyl]sulfanyl}acetate.

Methyl 2-{[3-(chloromethyl)-2-methylphenyl]sulfanyl}acetate

Methyl 2-{[3-(hydroxymethyl)-2-methylphenyl]sulfanyl}acetate, 4.4 g was dissolved in 220 mL methylene chloride, treated with thionyl chloride, 5 mL, and stirred at room temp. for 4 hours. The solvents were evaporated to yield 4.3 g of methyl 2-{[3-(chloromethyl)-2-methylphenyl]sulfanyl}acetate as a slightly brown oil.

Methyl 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetate

2-mercaptobenzimidazole, 2 g, was dissolved in a solution of 10 mL water, 30 mL methanol, and 0.53 g NaOH, and cooled on an ice bath. A solution of 3.2 g of methyl 2-{[3-(chloromethyl)-2-methylphenyl]sulfanyl}acetate in 50 mL methanol was added and the reaction was stirred at room temp. for 6 hours. The solvents were evaporated and the residue was partitioned between 600 mL CH_2Cl_2 and 300 mL of 5% Na_2CO_3, the org. layer was collected, dried over Na_2SO_4 and evaporated to give 3.1 g methyl 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetate as a light yellow solid.

2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol

Methyl 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetate, 5.7 g, was dissolved in 100 mL THF and cooled on a ice-bath. Lithium aluminum hydride, 0.5 g was added portion-wise under ca 5 min. After 30 min the reaction was quenched with Glauber salt($Na_2SO_4x10H_2O$). Filtration and evaporation afforded 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol, 4.1 g.

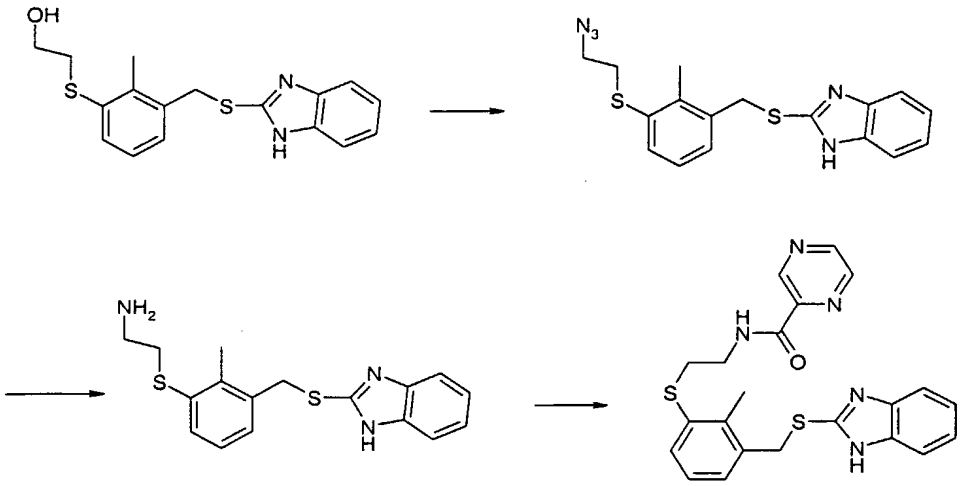
Mass spec.; M+H=331.

2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate

100 mg of 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol was dissolved in 2 mL DMF, and 35 mg phenyl isocyanate was added, the mixture was stirred for 18 hours at room temp., and concentrated in vacuo. Purification by reverse phase HPLC gave 60 mg 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}-sulfanyl)ethyl phenylcarbamate as a white solid.

Mass spec.; M+H=450.

Scheme 2



2-({3-[(2-Azidoethyl)sulfanyl]-2-methylbenzyl}sulfanyl)-1*H*-benzimidazole

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol, 0.165 g, triphenylphosphine, 0.184 g, and sodium azide, 0.13 g, were combined with stirring in 4 mL DMF on an ice bath, carbon tetrabromide, 0.25 g, was added, and the reaction was allowed to proceed for 18 hours. 20 mL methylene chloride was added, the resulting suspension was filtered, the solids were rinsed with methylene chloride and the filtrate washed with brine, dried over Na_2SO_4, and evaporated. Purification of the residue by flash chromatography (silica gel, EtOAc/Hexane = 1:5) gave 2-({3-[(2-azidoethyl)sulfanyl]-2-methylbenzyl}sulfanyl)-1*H*-benzimidazole, 0.85 g. Mass spec.; M+H=356

2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethylamine

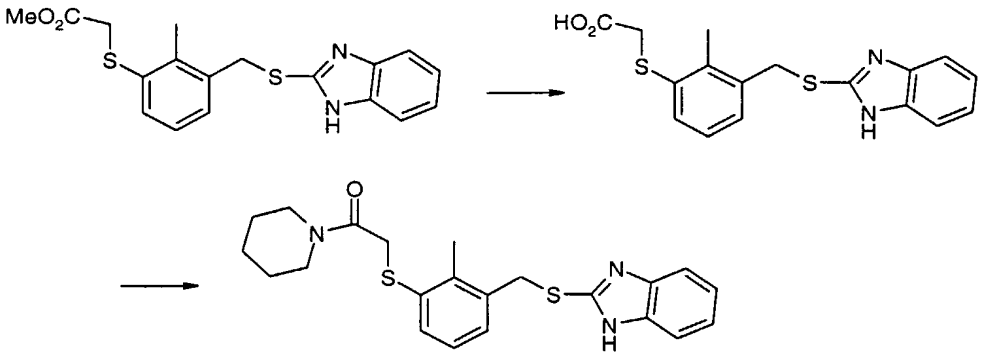
2-({3-[(2-azidoethyl)sulfanyl]-2-methylbenzyl}sulfanyl)-1*H*-benzimidazole, 0.42 g, was added to a suspension of 0.3 g lithium aluminum hydride in 10 mL THF over an ice bath. After 45 minutes, the reaction was quenched with $Na_2SO_4.10H_2O$ until H_2 evolution ceased.

The mixture was filtered, evaporated, dissolved in ethyl acetate and extracted with 1N HCl. The aqueous layer was washed with ethyl acetate and evaporated to give 275 mg of 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethylamine as a white solid. Mass spec.; M+H=330

***N*-[2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-pyrazinecarboxamide**

To a solution of 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethylamine (658 mg), 2-pyrazinecarboxylic acid (248 mg), diisopropylethylamine (1 mL) and DMF (8 mL) was added HBTU (829 mg). The resulting mixture was stirred overnight. The mixture was transferred to a sep. funnel and diluted with EtOAc (200 mL) and washed with water (2 x 100 mL). The organic layer was washed with Sat. Brine, dried over $MgSO_4$, filtered and concentrated. The crude residue was purified by reverse phase HPLC, C18 column (10-100% MeCN/H_2O) to give *N*-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-pyrazinecarboxamide as 600mg white solid. Mass spec.; M+H=436

Scheme 3



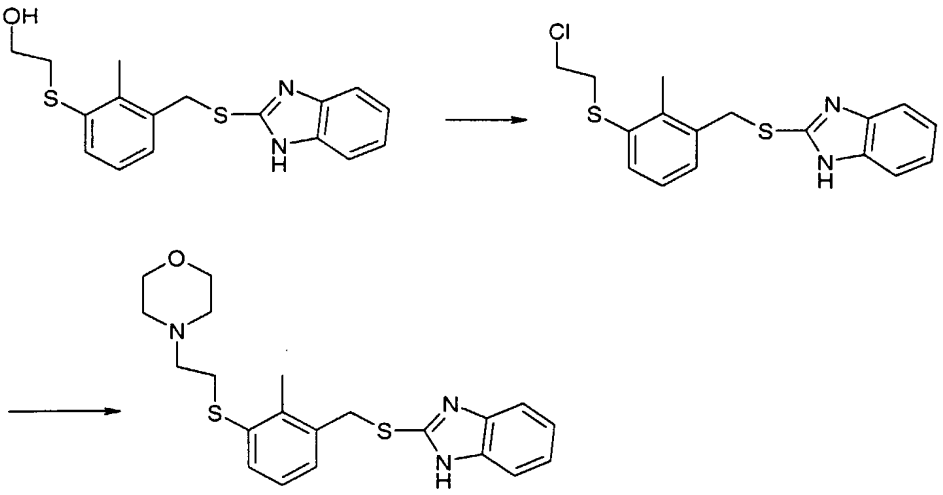
2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetic acid

Methyl 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetate, 0.68 g, was dissolved in 14 mL MeOH and treated with excess LiOH dissolved in 2 mL H_2O for 1 h. The solvents were evaporated and the residue was partitioned between 100 mL 5% Na_2CO_3 and 100 mL EtOAc. The aq layer was collected and the pH was adjusted to about 4 with 4M HCl. The aq layer was extracted with a 2:1 ethyl acetate/THF mixture. The combined organic layers were dried over $MgSO_4$ and evaporated to leave 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetic acid as a white solid, 0.5 g.

2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-(1-piperidinyl)-1-ethanone

100 mg of 2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetic acid was dissolved in 2 mL of DMF, 30 mg piperidine and 120 mg of HBTU were added. The mixture was stirred for 18 hours, diluted with ethyl acetate, washed with 5% $NaHCO_3$, saturated NaCl, dried over $MgSO_4$, and evaporated to give 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-(1-piperidinyl)-1-ethanone, 110 mg. Mass spec.; M+H=412.

Scheme 4



2-({3-[(2-Chloroethyl)sulfanyl]-2-methylbenzyl}sulfanyl)-1*H*-benzimidazole

0.38 g 2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol was combined with 5 mL CH_2Cl_2 and cooled to 0 °C. Excess $SOCl_2$ was added. Cold bath removed. Suspension stirred at RT for 2 hours. Concentrated in vacuo, 0.39 g crude 2-({3-[(2-chloroethyl)sulfanyl]-2-methylbenzyl}sulfanyl)-1*H*-benzimidazole obtained.

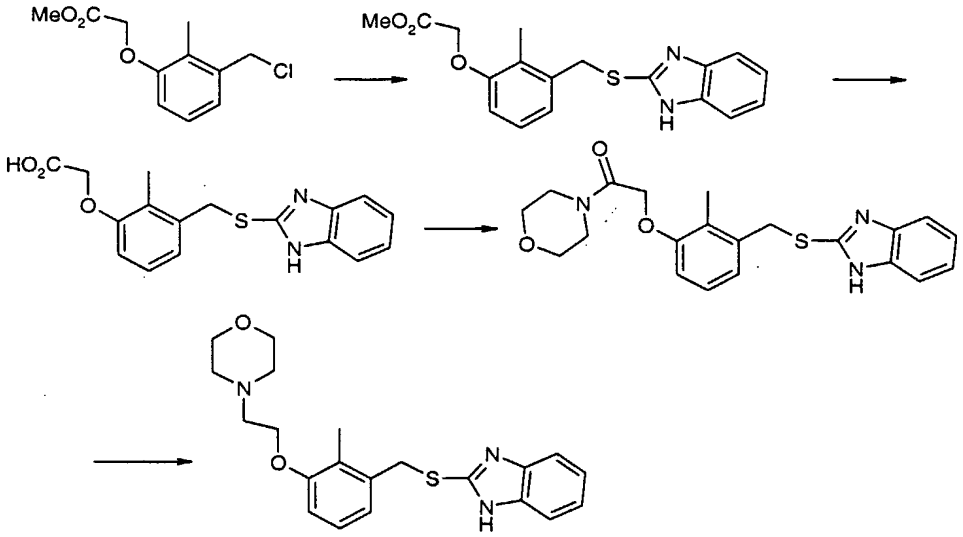
2-[(2-methyl-3-{[2-(4-morpholinyl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole

2-({3-[(2-Chloroethyl)sulfanyl]-2-methylbenzyl}sulfanyl)-1*H*-benzimidazole, 0.202 g, 1.3 mL morpholine, 3 mL DMF, and 1 mL DMSO combined and warmed at 80 °C for 1 day. Diluted to 100 mL with ethyl acetate. Washed with water, brine (2X), dried over $MgSO_4$, evaporated to give a thick oil. Purified via preparative HPLC to give 2-[(2-methyl-3-{[2-(4-morpholinyl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole as a fine powder, 0.12 g. Mass spec.; M+H=400.

Compound 113 can be prepared by a similar scheme by using 2-methyl-5-nitro-1*H*-imidazole in place of morpholine.

Compound 114 can be prepared by a similar scheme by using 1*H*-triazole in place of morpholine.

Scheme 5



Methyl 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}acetate

2-Mercaptobenzimidazole, 2 g, was dissolved in a solution of 10 mL water, 30 mL methanol, and 0.53 g NaOH, and cooled on an ice bath. A solution of 3.2 g of methyl 2-[3-(chloromethyl)-2-methylphenoxy]acetate in 50 mL methanol was added and the reaction was stirred at room temp. for 6 hours. The solvents were evaporated and the residue was partitioned between 600 mL CH_2Cl_2 and 300 mL of 5% Na_2CO_3, the org. layer was collected, dried over Na_2SO_4 and evaporated to give 3.1 g methyl 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}acetate as a light yellow solid.

2-{3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}acetic acid

Methyl 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}acetate, 0.68 g, was dissolved in 14 mL MeOH and treated with excess LiOH dissolved in 2 mL H_2O for 1 h. The solvents were evaporated and the residue was partitioned between 100 mL 5% Na_2CO_3 and 100 mL EtOAc. The aq layer was collected and the pH was adjusted to about 4 with 4M HCl. The aq layer was extracted with a 2:1 ethyl acetate/THF mixture. The combined organic layers were dried over $MgSO_4$ and evaporated to leave 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}acetic acid as a white solid, 0.5 g.

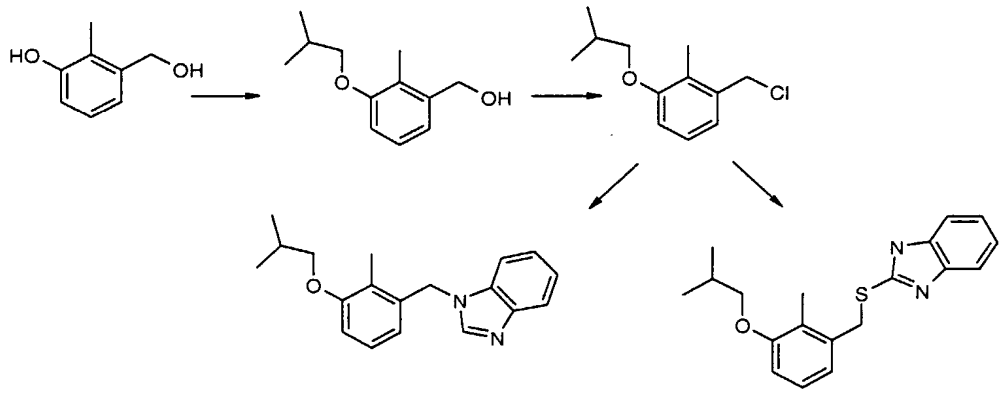
2-{3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}-1-(4-morpholinyl)-1-ethanone

100 mg of 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}acetic acid was dissolved in 2 mL of DMF, 30 mg morpholine and 120 mg of HBTU were added. The mixture was stirred for 18 hours, diluted with ethyl acetate, washed with 5% $NaHCO_3$, saturated NaCl, dried over $MgSO_4$, and evaporated to give 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}-1-(4-morpholinyl)-1-ethanone, 110 mg.

2-({2-Methyl-3-[2-(4-morpholinyl)ethoxy]benzyl}sulfanyl)-1*H*-benzimidazole

2-{3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenoxy}-1-(4-morpholinyl)-1-ethanone, 0.7 g, was dissolve in 20 mL THF. 0.2 g lithium aluminum hydride was added, and the mixtue was warmed to 70 °C for 45 minutes. Na_2SO_4-$10H_2O$ was added, the mixture was filtered, concentrated and purified by column chromatography (SiO_2 , ethyl acetate) to give 2-({2-methyl-3-[2-(4-morpholinyl)ethoxy]benzyl}sulfanyl)-1*H*-benzimidazole as a white foam, 0.42 g.

Scheme 6



(3-Isobutoxy-2-methylphenyl)methanol

2-Methyl-3-hydroxymethylphenol [prepared by lithium aluminum hydride reduction of 2-methyl-3-hydroxybenzoic acid], 1 g, isobutyl bromide, 1.6 mL, and K_2CO_3, 3 g, were combined in 10 mL DMF and stirred at 70 °C for 1 day. The mixture was diluted with ethyl acetate, washed with water and brine, dried over $MgSO_4$, and evaporated to give (3-isobutoxy-2-methylphenyl)methanol as a yellow waxy solid, 1.15 g.

1-(3-Isobutoxy-2-methylbenzyl)-1*H*-benzimidazole

0.5 g (3-isobutoxy-2-methylphenyl)methanol was dissolved in 3 mL CH_2Cl_2, and 0.7 mL $SOCl_2$ was carefully added. The mixture was stirred for 30 min., then concentrated to give crude 1-(chloromethyl)-3-isobutoxy-2-methylbenzene. The crude chloride sample was dissolved in 3 mL DMF, and 0.26 g benzimidazole and 0.6 g K_2CO_3 were added. The

suspension was stirred at rt overnight. The mixture was diluted with ethyl acetate, washed with water and brine, dried over $MgSO_4$, and evaporated to give a residue which was purified by flash chromatography, silica gel, 20-50% ethyl acetate/Hexane. 1-(3-isobutoxy-2-methylbenzyl)-1*H*-benzimidazole was thus obtained as an off-white solid, 0.6g. Mass spec.; M+H=295.

2-[(3-Isobutoxy-2-methylbenzyl)sulfanyl]-1*H*-benzimidazole

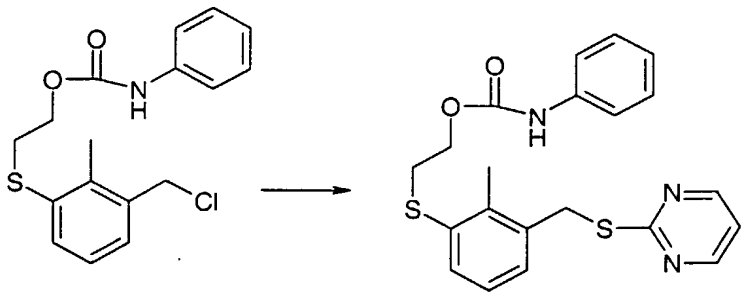
2-Mercaptobenzimidazole, 2 g, was dissolved in a solution of 10 mL water, 30 mL methanol, and 0.53 g NaOH, and cooled on an ice bath. A solution of 3.2 g 1-(chloromethyl)-3-isobutoxy-2-methylbenzene in 50 mL methanol was added and the reaction was stirred at room temp. for 6 hours. The solvents were evaporated and the residue was partitioned between 600 mL CH_2Cl_2 and 300 mL of 5% Na_2CO_3, the org. layer was collected, dried over Na_2SO_4 and evaporated to give 3.1 g 2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1*H*-benzimidazole as a light yellow solid.

Compound 105 can be made by a similar scheme by using 2-mercaptoindole in place of 2-mercaptobenzimidazole.

Compound 110 can be made by a similar scheme by using 2-mercaptobenzothiazole in place of 2-mercaptobenzimidazole.

Compound 111 can be made by a similar scheme by using 2-mercaptobenzoxazole in place of 2-mercaptobenzimidazole.

Scheme 7

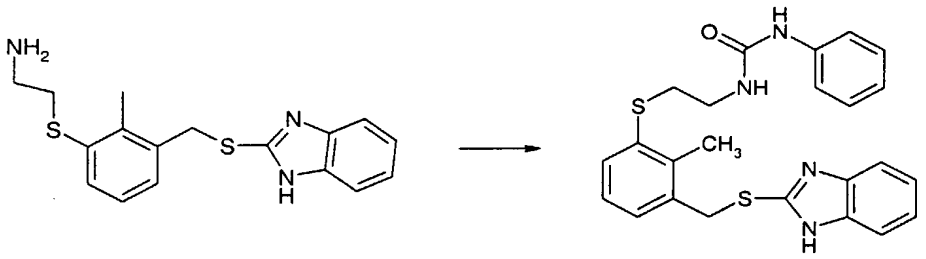


2-({2-Methyl-3-[(2-pyrimidinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate

To a solution of 135 mg of 2-{[3-(chloromethyl)-2-methylphenyl]sulfanyl}ethyl phenylcarbamate in 2 mL DMF was added 65 mg of 2-thiopyrimidine, and 600 mg K_2CO_3. The suspension was stirred vigorously at RT for 1.5 hrs. The mixture was diluted to 25 mL with ethyl acetate, washed with 15 mL water, 2 X 15mL 1N KOH, 15mL brine, and dried over $MgSO_4$. Evaporation gave a thick oil. Purification by flash chromatography, silica gel, 10-

30% ethyl acetate/hexane gave 2-({2-methyl-3-[(2-pyrimidinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate as a waxy solid, 130 mg. Mass spec.; M+H=412.

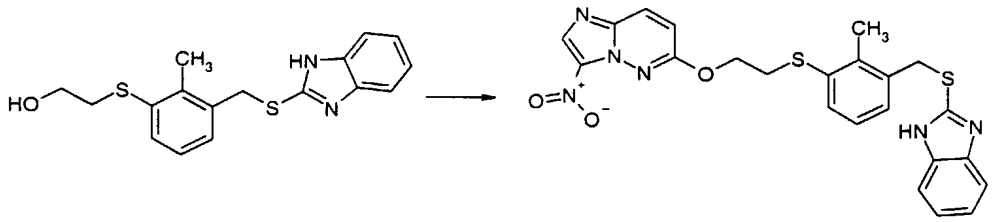
Scheme 8



***N*-[2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-*N'*-phenylurea**

100 mg of the 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanamine was dissolved in 2 mL of DMF and 36 mg of phenyl isocyanate was added. The mixture was stirred at rt overnight. The reaction was evaporated, and the crude compound was purified by reverse phase preparative HPLC to give *N*-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-*N'*-phenylurea as a white powder, 85 mg. Mass spec.; M+H=449.

Scheme 9

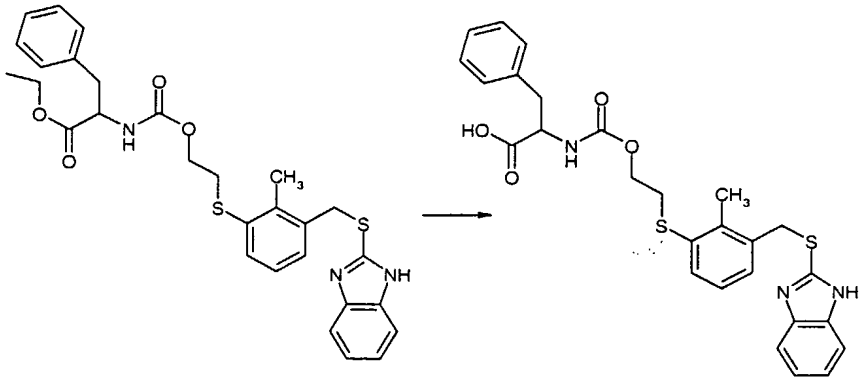


6-[2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]-3-nitroimidazo[1,2-*b*]pyridazine

To a solution of 330 mg of 2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol in 30 mL DMF was added 160 mg sodium hydride (60% dispersion in oil), the suspension was stirred for 30 min, then 199 mg of 6-chloro-3-nitroimidazo[1,2-*b*]pyridazine (Kobe, J.; Stanovnik, B.; Tisler, Miha. *Tetrahedron* (1968), 24(1), 239) was added. After stirring the suspension overnight at rt, 5 mL water was added carefully, then the mixture was concentrated under vacuum to leave a brown solid residue. The residue was stirred with acetone and filtered, the filtrate was concentrated and the resulting solids were rinsed with hot ethanol to yield 6-[2-({3-[(1*H*-benzimidazol-2-

ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]-3-nitroimidazo[1,2-*b*]pyridazine as a light brown powder, 140 mg.

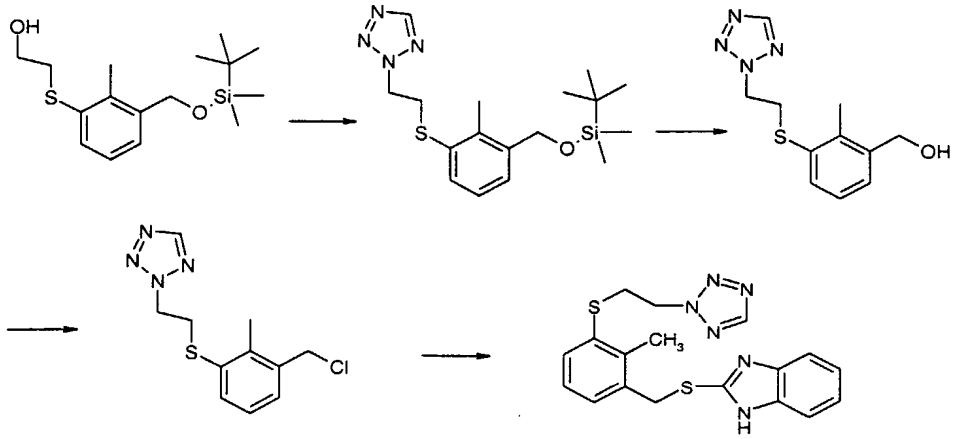
Scheme 10



***N*-{[2-({3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}phenylalanine**

25 mg of ethyl 2-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}-sulfanyl)ethoxy]carbonyl}amino)-3-phenylpropanoate was combined with 0.1 mL 1M KOH, and 0.5 mL dioxane to give a clear solution. After stirring for 1hr at rt the reaction was diluted with water, extracted twice with ethyl acetate, the aq layer was acidified with conc HCl and extracted three times with ethyl acetate. The organic layer was dried over $MgSO_4$ and evaporated to yield a clear oil. Trituration with 1:1 ether/hexane gave *N*-{[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}phenylalanine as a white solid: 20 mg. Mass spec.; M+H=522.

Scheme 11



2-(2-{[3-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2-methylphenyl]sulfanyl}ethyl)-2*H*-1,2,3,4-tetraazole

2-{[3-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2-methylphenyl]sulfanyl}-1-ethanol, 1.2 g, triphenylphosphine, 1.6 g, and tetrazole, 0.42 g, were combined in 10 mL THF to give a clear solution. The mixture was cooled to 0 °C, and 0.94 mL diethylazodicarboxylate was added. The reaction was allowed to slowly come to rt while stirring overnight. Evaporation and purification by flash chromatography, silica gel, 9:1 hexane : ethyl acetate, gave 2-(2-{[3-({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-2-methylphenyl]sulfanyl}ethyl)-2*H*-1,2,3,4-tetraazole as an oil, 770 mg.

(2-Methyl-3-{[2-(2*H*-1,2,3,4-tetraazol-2-yl)ethyl]sulfanyl}phenyl)methanol

2-(2-{[3-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2-methylphenyl]sulfanyl}ethyl)-2*H*-1,2,3,4-tetraazole, 770 mg, was dissolved in 20 mL THF and treated with 3 mL 75% aq. TBAF (tetrabutylammonium fluoride). The solution was stirred at rt overnight, concentrated, diluted with ethyl acetate, washed with 10% citric acid, then brine and dried over Na_2SO_4. Evaporation and purification by flash chromatography, silica gel, 1:1 hexane : ethyl acetate, gave (2-methyl-3-{[2-(2*H*-1,2,3,4-tetraazol-2-yl)ethyl]sulfanyl}phenyl)methanol, 500 mg.

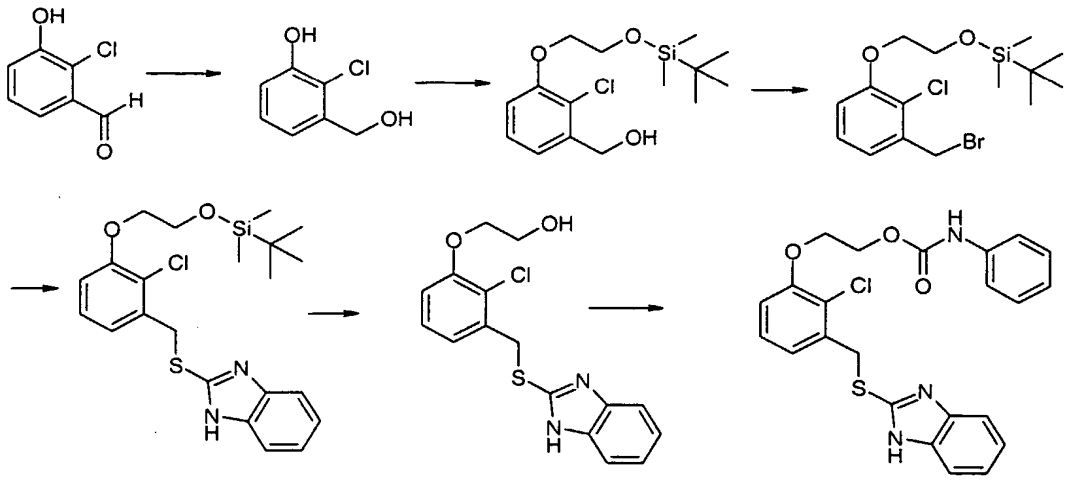
2-(2-{[3-(Chloromethyl)-2-methylphenyl]sulfanyl}ethyl)-2*H*-1,2,3,4-tetraazole

To a solution of 100 mg of (2-methyl-3-{[2-(2*H*-1,2,3,4-tetraazol-2-yl)ethyl]sulfanyl}phenyl)methanol in 4 mL methylene chloride at 0 °C was added 1 mL thionyl chloride. The cold bath was removed and the mixture was stirred at rt for 1.5 hrs. Evaporation to dryness gave 2-(2-{[3-(chloromethyl)-2-methylphenyl]sulfanyl}ethyl)-2*H*-1,2,3,4-tetraazole, 105 mg.

1*H*-Benzimidazol-2-yl 2-methyl-3-{[2-(2*H*-1,2,3,4-tetraazol-2-yl)ethyl]sulfanyl}benzyl sulfide

2-(2-{[3-(chloromethyl)-2-methylphenyl]sulfanyl}ethyl)-2*H*-1,2,3,4-tetraazole, 105 mg, was dissolved in 2 mL DMF, 1 g K_2CO_3 and 100 mg 2-thiobenzimidazole were added and the suspension was stirred at rt overnight. The mixture was diluted with water, extracted with methylene chloride, washed with brine, dried over $MgSO_4$, and evaporated. Purification by flash chromatography, silica gel, 1.5 : 1 ethyl acetate : hexane gave 1*H*-benzimidazol-2-yl 2-methyl-3-{[2-(2*H*-1,2,3,4-tetraazol-2-yl)ethyl]sulfanyl}benzyl sulfide as an off-white solid, 70 mg. Mass spec.; M+H=383.

Scheme 12



2-Chloro-3-(hydroxymethyl)phenol

2 g 2-chloro-3-hydroxybenzaldehyde (Ginsburg, D. *J.Amer.Chem.Soc.* 1951(73), 702) was dissolved in 30 mL THF / 10 mL methanol / 20 mL 1N KOH. 1 g $NaBH_4$ was added. After stirring at RT for 1.5 hrs, the mixture was diluted with water and extracted with ether (2X). The aqueous layer was acidified with conc. HCl, and extracted with ethyl acetate (2X). The pooled ethyl acetate layer was dried over $MgSO_4$ and evaporated to give 2-chloro-3-(hydroxymethyl)phenol as a white solid, 2.02 g.

[3-(2-{[*tert*-Butyl(dimethyl)silyl]oxy}ethoxy)-2-chlorophenyl]methanol

2-Chloro-3-(hydroxymethyl)phenol, 0.317 g, K_2CO_3, 0.264 g, and (2-bromoethoxy)(*tert*-butyl)dimethylsilane, 0.429 mL, were combined in 10 mL acetonitrile. The suspension was refluxed for 18 hrs, and an additional 0.2 mL (2-bromoethoxy)(*tert*-butyl)dimethylsilane was added. After refluxing the mixture an additional 24 hrs, it was filtered, and evaporated to give a crude residue. Purification by column chromatography (8:2 hexane : ethyl acetate) gave [3-(2-{[*tert*-butyl(dimethyl)silyl]oxy}ethoxy)-2-chlorophenyl]methanol as a clear oil, 0.42 g.

{2-[3-(Bromomethyl)-2-chlorophenoxy]ethoxy}(*tert*-butyl)dimethylsilane

N-bromosuccinimide, 0.47 g, was dissolved in 20 mL methylene chloride and cooled to 0 °C. Dimethylsulfide, 0.213 mL, was added slowly and the mixture was stirred for 30 minutes at 0 °C. A solution of 0.42 g [3-(2-{[*tert*-butyl(dimethyl)silyl]oxy}ethoxy)-2-chlorophenyl]methanol in 5 mL methylene chloride was added, and the reaction was allowed to proceed at RT for 2 h. The mixture was concentrated to give crude {2-[3-(bromomethyl)-2-

chlorophenoxy]ethoxy}(*tert*-butyl)dimethylsilane, 0.56 g, used in the next step without any further purification.

2-{[3-(2-{[*tert*-Butyl(dimethyl)silyl]oxy}ethoxy)-2-chlorobenzyl]sulfanyl}-1*H*-benzimidazole

0.5 g {2-[3-(bromomethyl)-2-chlorophenoxy]ethoxy}(*tert*-butyl)dimethylsilane was combined with 0.2 g benzimidazole and 4 mL 1 M NaOH in 12 mL ethanol. The solution was stirred for 2.5 hrs, and the ethanol was evaporated to yield a slurry. Dilution with ethyl acetate, extraction with water, then sat. NaCl gave a clear solution. The solution was dried over $MgSO_4$, and evaporated to give 2-{[3-(2-{[*tert*-butyl(dimethyl)silyl]oxy}ethoxy)-2-chlorobenzyl]sulfanyl}-1*H*-benzimidazole as a white foam, 0.53 g.

2-{3-[(1*H*-Benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}-1-ethanol

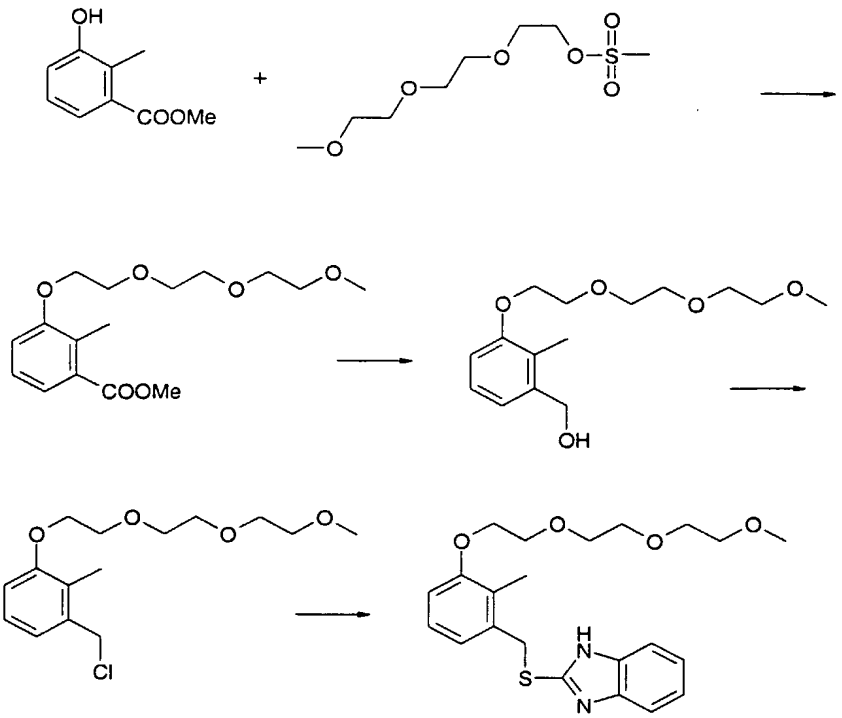
0.53 g 2-{[3-(2-{[*tert*-butyl(dimethyl)silyl]oxy}ethoxy)-2-chlorobenzyl]sulfanyl}-1*H*-benzimidazole was dissolved in 10 mL THF and 0.52 mL 2.73 M aqueous tetrabutylammonium fluoride was added. The solution was stirred for 2 hrs, diluted with water, and extracted with ethyl acetate. The organic phase was washed with sat. NaCl, dried over $MgSO_4$ and evaporated to yield 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}-1-ethanol as 0.4 g white foamy oil.

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}ethyl phenylcarbamate

0.4 g 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}-1-ethanol was dissolved in 5 mL chloroform and 0.15 mL phenyl isocyante was added. The mixture was stirred at RT for 2 hrs, diluted with chloroform, washed with water, and sat. NaCl. The solution was dried over $MgSO_4$ and evaporated to yield 2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}ethyl phenylcarbamate as 0.52g white solid.

Compounds 119 and 120 can be made by a similar route, but using 2-methoxy-3-(hydroxymethyl)phenol (see Chemistry Letters, 1986,871) in place of 2-chloro-3-(hydroxymethyl)phenol.

Scheme 13



Methyl 2-methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethoxy]benzoate

Methyl 2-methyl-3-hydroxybenzoate [Fringuelli, F.; Mancini, V.; Taticchi, A. *Tetrahedron*, **1969**, *25*, 4249] (0.5 g) was dissolved in 10 mL MeCN, anhydrous K_2CO_3 (1 g) was added followed by 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate [prepared by reaction of the corresponding alcohol with methanesulfonyl chloride] (1.09 g). The mixture was allowed to react at reflux over night, cooled, filtered, and taken to dryness. The residue was dissolved in CH_2Cl_2 and washed with diluted NaOH (aq) and brine. The organic layer was collected, dried, and evaporated furnishing 0.56g of the title compound which was used without further purification.

2-Methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethoxy]benzyl alcohol

A solution of Methyl 2-methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethoxy]benzoate (2.1 mmol) in THF (10 mL) was gently added to a stirred suspension of $LiAlH_4$ (4.5 mmol) in 20 mL THF, then heated to reflux for 2 hours. The reaction was quenched with 0.25 mL water, 0.5 mL 2M NaOH, and 0.25 mL water. The mixture was refluxed for another hour and then filtered to remove the solids. The filtrate was evaporated affording 0.28 g of the title compound.

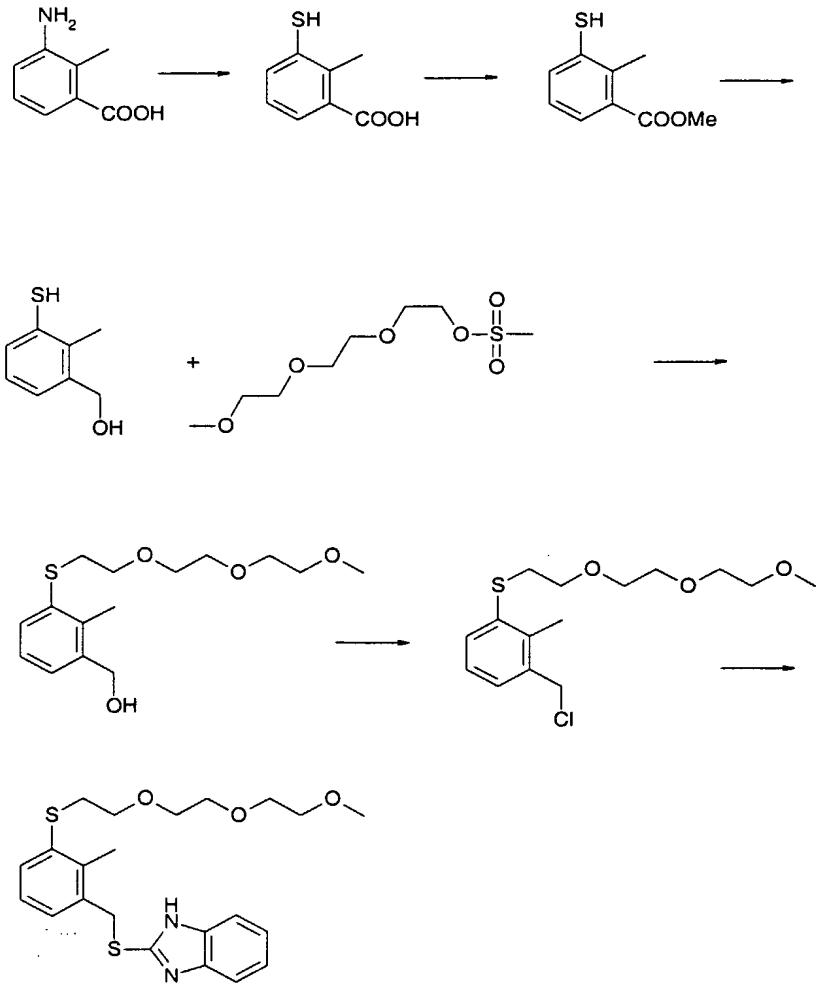
2-Methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethoxy]benzyl chloride

2-Methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethoxy]benzyl alcohol (1.1 mmol) was dissolved 5 mL CH_2Cl_2 and treated with 0.2 mL $SOCl_2$ for 30 min at ambient temperature. The solvent and excess reagent were evaporated leaving a quantitative yield of the title compound which was used immediately in the next step.

2-[(3-{2-[2-(2-Methoxyethoxy)ethoxy]ethoxy}-2-methylbenzyl)sulfanyl]-1*H*-benzimidazole

2-mercaptobenzimidazole (0.18 g, 1.18 mmol), suspended in 3 mL MeOH, was treated with 2 M NaOH (1.3 mL, 2.6 mmol) and allowed to form a solution. 2-Methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethoxy]benzyl chloride (0.33 g, 1.08 mmol) was added and reacted for 18 h at ambient temperature. The solvents were evaporated and the residue partitioned between water and CH_2Cl_2 (4 x 25 mL). The organic layers were combined, dried, and evaporated. Reverse phase preparative LC afforded 115 mg (26%) of the title compound. Compound 107 can be prepared by a similar scheme by replacing 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate with 3,6,9,12,15-pentaoxahexadec-1-yl methanesulfonate.

Scheme 14



2-Methyl-3-mercapto-benzoic acid

3-Amino-2-methylbenzoic acid, 11.3 g, was dissolved in H_2O (100 mL) and conc. HCL (15 mL) was added at 0 °C. $NaNO_2$ (5.5g) in H_2O (40 mL) was added to the above suspension over 30min. The above diazonium salt was kept at 0 °C and added slowly (over 40 min) to a solution of potassium ethylxanthogenate (14 g) while the pH continually was adjusted to 8 with Na_2CO_3. The mixture was stirred for 30 minutes, cooled to ambient temperature, and poured onto a mixture of 300 mL concentrated HCl and 700 mL of ice water. The precipitate was collected, taken up in water (300 mL), and treated with NaOH (6 g) at reflux for 20 h. The mixture was poured onto a mixture of 40 mL concentrated HCl in 300 mL ice water and extracted with 3 × 500 mL CH_2Cl_2. The combined organic layers were dried and evaporated furnishing 7 g of the title compound as yellow crystals (which slowly oxidized to the corresponding disulfide upon standing)

2-Methyl-3-mercapto-methylbenzoate

2-Methyl-3-mercapto-benzoic acid (14.7 g) was dissolved in 250 mL of MeOH and a few drops of conc. H_2SO_4 was added. The mixture was heated to reflux for 48 hours and then allowed to cool to ambient temperature before the bulk MeOH was evaporated. The residue was dissolved in Et_2O and washed with 4 x 50 mL H_2O and 50 mL brine. The organic layer was collected, dried, and evaporated leaving 14.8 g of the title compound as a viscous yellow oil (which slowly oxidized to the corresponding disulfide upon standing.

2-Methyl-3-mercapto-benzylalcohol

A solution of 2-Methyl-3-mercapto-methylbenzoate (2.0 g) in THF (5 mL) was added drop wise to a suspension of $LiAlH_4$ (1.32 g) in THF (100 mL) under dry and inert conditions. The mixture was heated to reflux for 2 h and then quenched with 2 mL of water, 4 mL of 2 M NaOH, and another 2 mL of water. After refluxing for another hour, solids were filtered off and washed with THF and methanol. The combined filtrates were evaporated and the residue partitioned between 2M HCl and EtOAc. The organic layer was collected, dried, and evaporated to yield 1.9 g 2-Methyl-3-mercapto-benzylalcohol, contaminated with the corresponding disulfide as an oil. This material could be used in the next step without further purification.

2-Methyl-3-(2-(2-(2-methoxyethoxy)ethoxy)ethylthio)benzyl alcohol

A mixture of 2-Methyl-3-mercapto-benzylalcohol and its disulfide (50 mg, 0.325 mmol monomer) in dioxane/water (4/1) (1 mL) and a small amount of concentrated HCl was reacted with PPh_3 (26 mg, 0.1 mmol) for 1 h at ambient temperature in an inert atmosphere. The solvents were removed and the residue taken up in MeCN (1 mL) and reacted with Et_3N (290 mL, 2.08 mmol) and 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate [prepared by reaction of the corresponding alcohol with methanesulfonyl chloride] (0.30 g, 1.24 mmol) for 3 days at ambient temperature. The solvent was evaporated and the residue partitioned between EtOAc and water. The organic layer was collected, dried, and taken to dryness. The product was purified on silica gel (pentane/Et_2O; 6/4 to 0/10) furnishing 50 mg of the title compound as a colorless oil.

2-Methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethylthio]benzyl chloride

2-Methyl-3-(2-(2-(2-methoxyethoxy)ethoxy)ethylthio)benzyl alcohol (0.17 mmol) was dissolved in 2 mL CH_2Cl_2 and treated with 0.1 mL $SOCl_2$ for 30 min at ambient temperature. The solvent and excess reagent were evaporated leaving a quantitative yield of the title compound which was used immediately in the next step.

2-{[3-({2-[2-(2-Methoxyethoxy)ethoxy]ethyl}sulfanyl)-2-methylbenzyl]sulfanyl}-1*H*-benzimidazole

2-Mercaptobenzimidazole (0.33 g, 2.16 mmol), suspended in 6 mL MeOH, was treated with 2 M NaOH (2.6 mL) and allowed to form a solution. 2-Methyl-3-[2-(2-(2-methoxyethoxy)ethoxy)ethylthio]benzyl chloride (0.58 g, 1.80 mmol) was added and reacted for 18 h at ambient temperature. The solvents were evaporated and the residue partitioned between water and CH_2Cl_2 (4 x 25 mL). The organic layers were combined, dried, and evaporated. Reverse phase preparative LC afforded 0.47 g of the title compound.

Compound 109 can be prepared by a similar scheme by replacing 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate with 3,6,9,12,15-pentaoxahexadec-1-yl methanesulfonate.

Compound 112 can be prepared by a similar scheme by replacing 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate with isobutyl bromide.

Compound 115 can be prepared by a similar scheme by replacing 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate with 3,6,9,12,15-pentaoxahexadec-1-yl methanesulfonate, and 2-mercaptobenzimidazole replaced with 5-carboethoxy-2-mercaptobenzimidazole.

Compound 116 can be prepared by a similar scheme by replacing 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate with 3,6,9,12,15-pentaoxahexadec-1-yl methanesulfonate, and 2-mercaptobenzimidazole replaced with 5-(propan-1-one)-2-mercaptobenzimidazole.

Compound 117 can be prepared by a similar scheme by replacing 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate with 3,6,9,12,15-pentaoxahexadec-1-yl methanesulfonate, and 2-mercaptobenzimidazole replaced with 5-amino-2-mercaptobenzimidazole.

Compound 118 can be prepared by a similar scheme by replacing 2-[2-(2-methoxyethoxy)ethoxy]ethyl methanesulfonate with 3,6,9,12,15-pentaoxahexadec-1-yl methanesulfonate, and 2-mercaptobenzimidazole replaced with 5-(hydroxymethyl)-2-mercaptobenzimidazole.

Table 1 shows which compounds can be made by each of Schemes 1 to 14 or by schemes that are similar to schemes 1 to 14, but differ in one or more reagents as will be readily apparent to the skilled person taking into account the final compound.

Table 1

SCHEME	COMPOUND NO.
1	1-37
2	38-54
3	55-82
4	83, 84, 113, 114
5	104
6	103, 105, 110, 111
7	85-96
8	97, 98
9	99
10	100
11	101, 102
12	119-122
13	106, 107
14	108, 109, 112, 115-118

ASSAYS

Microdilution assay

The microdilution assay tests the anti-*H. pylori* activity of compounds. In this assay, MICs (Minimum Inhibitory Concentrations) were determined against four *H. pylori* strains, including ATCC 43504, that exhibit different susceptibilities to known antibiotics. The tests were performed in 24-well microtiter plates in which the medium, the inoculum, and the antibiotic solutions were distributed in the wells. Serial dilutions were prepared in 24-well plates containing a total volume of 2 mL medium per well. Cultures were resuspended in Brucella broth (OD_{600} of 0.6) and 50 µl of these cultures were inoculated into each well to give a final concentration of 10^7 cells per mL (OD_{600} of less than 0.03, which is the same as that of the non-inoculated control). The plates were then incubated for two days and the amount of growth recorded (OD_{600}) with a plate reader (Molecular Devices, Sunnyvale, California). The plates were incubated in a controlled microaerophilic atmosphere (5% O_2, 10% CO_2 and 85% N_2) that assured optimal growth of the bacterial strains and high

reproducibility of results. The MIC was defined as the lowest concentration of antibiotic resulting in complete inhibition of growth.

MIC values <10μg/mL are indicative of anti-*Helicobacter pylori* activity. Compounds according to the invention were tested in this assay and give MIC values in this range.

Selectivity Assays

Standard agar dilution protocols were used to determine the effect of compounds of the invention on panels of Gram negative and Gram positive bacteria. The effects on both aerobic ["Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically-Fourth Edition; Approved Standard" NCCLS Document M7-A4 Vol. 17 No. 2, January 1997] and anaerobic ["Methods for Antimicrobial Susceptibility Testing of anaerobic Bacteria -Third Edition; Approved Standard" NCCLS Document M11-A3 Vol. 13 No. 26, December 1993] organisms were measured. Compounds of the invention had no effect in these assays at concentrations of greater than ten times the corresponding MICs determined vs. *Helicobacter pylori* in the microdilution assay.

The invention relates in one aspect to a compound of formula I for use as a medicament. The compound can be provided as part of a pharmaceutical formulation which alo includes a pharmaceutically acceptable diluent or carrier (e.g., water). The formulation may be in the form of tablets, capsules, granules, powders, syrups, emulsions (e.g., lipid emulsions), suppositories, ointments, creams, drops, suspensions (e.g., aqueous or oily suspensions) or solutions (e.g., aqueous or oily solutions). If desired, the formulation may include one or more additional substances independently selected from stabilising agents, wetting agents, emulsfying agents, buffers, lactose, sialic acid, magnesium stearate, terra alba, sucrose, corn starch, talc, gelatin, agar, pectin, peanut oil, olive oil, cacao butter and ethylene glycol. The formulation may contain or be co-administered with one or more known drugs selected from other clinically useful antibacterial agents.

The compound is preferably orally administered to a patient, but other routes of administration are possible, such as parenteral or rectal administration. For intravenous, subcutaneous or intra-muscular administration, the patient may receive a daily dose of 5 $mgkg^{-1}$ to 20 $mgkg^{-1}$ of the compound, the compound being administered 1 to 4 times per day. The intravenous, subcutaneous and intra-muscular dose may be given by means of a bolus injection. Alternatively, the intravenous dose may be given by continuous infusion over a period of time. Alternatively, the patient may receive a daily oral dose which is

approximately equivalent to the daily parenteral dose, the composition being administered 1 to 4 times per day. A suitable pharmaceutical formulation is one suitable for oral administration in unit dosage form, for example as a tablet or capsule, which contains between 100mg and 1g of the compound of the invention.

The following illustrate representative pharmaceutical dosage forms containing the compound of the invention, or a pharmaceutically acceptable salt or solvate thereof (hereafter referred to as "compound X"), for therapeutic or prophylactic use in humans.

(a)

Tablet I	mg/tablet
Compound X.	100
Lactose Ph.Eur.	179
Croscarmellose sodium	12.0
Polyvinylpyrrolidone	6
Magnesium stearate	3.0

(b)

Tablet II	mg/tablet
Compound X	50
Lactose Ph.Eur.	229
Croscarmellose sodium	12.0
Polyvinylpyrrolidone	6
Magnesium stearate	3.0

(c)

Tablet III	mg/tablet
Compound X	1.0
Lactose Ph.Eur.	92
Croscarmellose sodium	4.0
Polyvinylpyrrolidone	2.0
Magnesium stearate	1.0

(d)

Capsule	mg/capsule
Compound X	10
Lactose Ph.Eur.	389
Croscarmellose sodium	100
Magnesium stearate	1.

(e)

Injection I	(50 mg/mL)
Compound X	5.0% w/v
Isotonic aqueous solution	to 100%

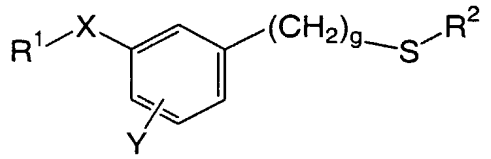
Buffers, pharmaceutically acceptable co-solvents (e.g., polyethylene glycol, propylene glycol, glycerol or EtOH) or complexing agents such as hydroxy-propyl β cyclodextrin may be used to aid formulation.

Another aspect of the invention relates to the use of a compound of formula I, in the manufacture of a medicament, for the therapeutic and/or prophylactic treatment of *Helicobacter pylori* infection in a mammalian host, e.g. a human. By "therapeutic treatment", we mean the eradication or suppression of a pre-existing *Helicobacter pylori* infection in the host.

In a further aspect of the invention, there is provided a method of therapeutically treating or preventing *Helicobacter pylori* infection in a mammal (e.g., a human), the method comprising administering (e.g., orally) to the mammal a compound of formula I or a pharmaceutical formulation as described above. By "therapeutically treating", we mean bringing about the eradication or suppression of a pre-existing *Helicobacter pylori* infection in the host.

CLAIMS:

1. A compound of formula I or a pharmaceutically acceptable salt or solvate thereof



I

wherein:

X is S; SO_2; NH; N(C_{1-6}alkyl); O or CH_2;

Y is C_{1-6}alkyl; O(C_{3-8}cycloalkyl); O(C_{1-6}alkyl); Hal; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal, wherein Hal represents halogen; NRR´, wherein R and R´ independently represent H or C_{1-8}alkyl, or NRR´ represents an optionally substituted C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S; H; COOR″ or COR″, R″ representing H or C_{1-6}alkyl; or CH_2OH;

R^1 is $-(CH_2)_a-R^3$; $-((CH_2)_bO)_c-R^3$; $-(CH_2)_d-R^{3'}$; $-(CH_2)_aC(=O)R^3$; $-(CH_2)_dC(=O)R^{3'}$; $-((CH_2)_e-O)_{c'}-(CH_2)_f-R^{3'}$; R^3 or $R^{3'}$;

R^2 is an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S;

R^3 is H; C_{1-6}alkyl; optionally substituted C_{3-8}cycloalkyl optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or an optionally substituted 5- to 10-membered mono- or bi-cyclic heterocyclic ring structure containing 1, 2, 3, 4 or 5 heteroatoms independently selected from O, N and S;

$R^{3'}$ is -Z-M wherein Z represents O, S or NH and M represents H, an optionally substituted mono- or bi- cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, or an optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or -Z-M represents $-C(=O)NR^6R^7$, $-NR^6R^7$, $-OC(=O)NR^8R^9$, $-NC(=O)NR^8R^9$ or $-NC(=O)R^8$;

For R^6 and R^7, either:

(i) R^6 is H; C_{1-12}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; optionally substituted (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10}; optionally substituted (C_{1-8}alkyl)R, where R represents a mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered

heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S or R represents a mono-, bi- or tri-cyclic C_{3-13}cycloalkyl; optionally substituted C_{6-10}aryl; an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; or -C(=O)-O-Ar, wherein Ar represents optionally substituted C_{6-10}aryl; and

R^7 is H; or

(ii) the structure $-NR^6R^7$ represents a C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S, $-NR^6R^7$ being optionally substituted;

a represents an integer 1, 2, 3, 4 or 5;

each b independently represents an integer 1, 2, 3, 4 or 5;

c represents an integer 1, 2, 3, 4 or 5;

c' represents an integer 1, 2, 3, 4 or 5;

d represents an integer 1, 2, 3, 4 or 5;

each e independently represents an integer 1, 2, 3, 4 or 5;

f represents an integer 1, 2, 3, 4 or 5; and

g represents zero or an integer 1, 2, 3, 4 or 5;

or a pharmaceutically acceptable salt or solvate thereof.

2. A compound according to Claim 1, wherein:

a is 1, 2 or 3;

b is 2;

c' is 1, 2, 3, 4 or 5;

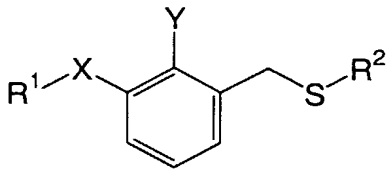
d is 1, 2 or 3;

e is 2;

f is 1, 2 or 3; and

g is 1 or 2.

3. A compound according to Claim 2, having the general structure Ib



Ib

wherein:

X is S, S(=O), $S(=O)_2$ or O;

Y is C_{1-6}alkyl, $O(C_{1-6}alkyl)$, Hal; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal;

R^1 is $-(CH_2)_a-R^3$, $-((CH_2)_2O)_c-R^3$, $-(CH_2)_d-R^{3'}$, $-(CH_2)_aC(=O)R^3$, $-(CH_2)_dC(=O)R^{3'}$, $-((CH_2)_2O)_{c'}-(CH_2)_f-R^{3'}$;

R^3 is C_{1-6}alkyl; optionally substituted C_{3-8}cycloalkyl optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or an optionally substituted 5- to 10-membered mono- or bi-cyclic heterocyclic ring structure containing 1, 2, 3, 4 or 5 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle;

$R^{3'}$ is -Z-M wherein Z represents O, S or NH and M represents H, an optionally substituted mono- or bi- cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; or an optionally substituted C_{5-10} aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or -Z-M represents $-C(=O)NR^6R^7$, $-NR^6R^7$, $-OC(=O)NR^8R^9$, $-NC(=O)NR^8R^9$ or $-NC(=O)R^8$;

For R^6 and R^7, either:

(i) R^6 is H; C_{1-12}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; optionally substituted $(C_{1-8}alkyl)$aryl wherein the aryl is C_{6-10}; optionally substituted $(C_{1-8}alkyl)R$, where R represents a mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; or R represents a mono-, bi- or tri-cyclic C_{3-13}cycloalkyl; optionally substituted C_{6-10}aryl; an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; or -C(=O)-O-Ar, wherein Ar represents optionally substituted C_{6-10}aryl; and

R^7 is H; or

(ii) the structure $-NR^6R^7$ represents a C_{3-8} heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S per cycle; $-NR^6R^7$ being optionally substituted;

or a pharmaceutically acceptable salt or solvate thereof.

4. A compound according to Claim 3, wherein:

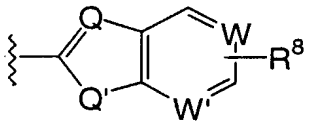
X is S or O;

R^1 is $-(CH_2)_2R^3$, $-(CH_2)_2R^{3'}$, $-CH_2C(=O)R^3$ or $-CH_2C(=O)R^{3'}$; and

R^3 is optionally substituted C_{3-8}cycloalkyl optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; optionally substituted C_{5-10}aromatic ring structure optionally containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or an optionally substituted 5- to 10-membered mono- or bi-cyclic heterocyclic ring structure containing 1, 2, 3, 4 or 5 heteroatoms independently selected from O, N and S.

5. A compound according to either Claim 1, 2 or 3, wherein R^1 is selected from *-iso*-Bu, $-(CH_2CH_2O)_3CH_3$, $-(CH_2CH_2)$-4-morpholinyl, $-(CH_2CH_2O)_5CH_3$, $-(CH_2CH_2)$-1-(2-methyl-5-nitro-imidazolyl), $-(CH_2CH_2)$-1-(1,2,4-triazolyl), and $-(CH_2CH_2)$-OC(=O)NH-Ph.

6. A compound according to any one of Claims 1, 2 or 3, wherein R^2 represents



wherein:

Q is CH or N;

Q´ is NH, O or S;

W is CH or N;

W´ is CH or N; and

R^8 is C_{1-6}alkyl; O(C_{3-8}cycloalkyl); O(C_{1-6}alkyl); Hal; $CHal_3$, $CHHal_2$, CH_2Hal, $OCHal_3$, $OCHHal_2$ or OCH_2Hal, wherein Hal represents halogen; NRR´, wherein R and R´ independently represent H or C_{1-8}alkyl, or NRR´ represents an optionally substituted C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently

selected from O, N and S, wherein the heterocyclic ring contains at least one carbon atom and contains no more than one O and no more than one S; H; $COOR^9$ or COR^9, R^9 representing H or C_{1-6}alkyl; or CH_2OH.

7. A compound of Claim 1, wherein R^1 is $-(CH_2)_a-CH_3$ or $-((CH_2)_bO)_c-CH_3$.

8. A compound according to Claim 2, wherein $R^{3'}$ is selected from -4-morpholinyl, -1-(2-methyl-5-nitro-imidazolyl), -1-(1,2,4-triazolyl) and -OC(=O)NH-Ph.

9. A compound according to any one of Claims 1 through 8, wherein g is 1.

10. A compound of Claim 1, wherein the compound is selected from:
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-ethanol;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl isopropylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-phenoxyphenylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl pentylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2,5-dimethylphenylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl (1*S*,2*R*)-2-phenylcyclopropylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl cyclohexylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-(methylsulfanyl)phenylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenethylcarbamate;
2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2-(2-thienyl)ethylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl methylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2-methylphenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-methoxyphenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-fluorophenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl benzylcarbamate;

methyl 3-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}amino)benzoate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,4-dichlorobenzylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,4-difluorophenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenyl dicarbonimidoate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-bromophenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-methylbenzylcarbamate;

ethyl 2-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}amino)-3-phenylpropanoate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,5-dimethyl-4-isoxazolylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3-acetylphenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl benzoylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-chloro-2-methylphenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-methoxybenzylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,4-dichlorophenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-(dimethylamino)phenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2,5-dichlorophenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 3,5-dimethoxyphenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2,4-dimethoxyphenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl (1*R*)-1-phenylethylcarbamate;

ethyl 4-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}amino)benzoate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 2-ethylphenylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl 4-fluorobenzoylcarbamate;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethylamine;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]benzamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]cyclohexanecarboxamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-[(4*S*)-2,5-dioxoimidazolidinyl]acetamide;

tert-butyl 4-({[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]amino}carbonyl)-1-piperidinecarboxylate;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-pyrazinecarboxamide;

2-(1-adamantyl)-*N*-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]acetamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7*H*-purin-7-yl)acetamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-furamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-5-nitro-2-furamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-2-thiophenecarboxamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-1-benzofuran-2-carboxamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-1-ethyl-3-methyl-1*H*-pyrazole-5-carboxamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]nicotinamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-4-quinolinecarboxamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-3,5-dimethyl-4-isoxazolecarboxamide;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-5-isoxazolecarboxamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-cyclopropylacetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(1,3-benzodioxol-5-ylmethy)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-(1-piperidinyl)-1-ethanone;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2-furylmethyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-cyclohexylacetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(tetrahydro-2-furanylmethyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-cyclopentylacetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2-thienylmethyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-[2-(4-morpholinyl)ethyl]acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2,3-dihydro-1*H*-inden-2-yl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-benzylacetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(2,5-dimethoxyphenethyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-[2-(2-pyridinyl)ethyl]acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-[2-(1-methyl-2-pyrrolidinyl)ethyl]acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(3,3-diphenylpropyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-phenethylacetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(4-methoxyphenethyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-hexylacetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-isobutylacetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(4-pyridinylmethyl)acetamide;

N'-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)acetyl]-2-furohydrazide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-octahydro-1(2*H*)-quinolinyl-1-ethanone;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(benzyloxy)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-[4-(2-methoxyphenyl)-1-piperazinyl]-1-ethanone;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-[6,7-dimethoxy-3,4-dihydro-2(1*H*)-isoquinolinyl]-1-ethanone;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-*N*-(4-butylphenyl)acetamide;

2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)-1-(4-methyl-1-piperazinyl)-1-ethanone;

2-[(2-methyl-3-{[2-(4-morpholinyl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole;

2-[(2-methyl-3-{[2-(4-methyl-1-piperazinyl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole;

2-({3-[(1*H*-imidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate;

2-[(2-methyl-3-{[(5-phenyl-1,3,4-oxadiazol-2-yl)sulfanyl]methyl}phenyl)sulfanyl]ethyl phenylcarbamate;

2-({2-methyl-3-[(2-pyrimidinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate;

2-[(2-methyl-3-{[(1-phenyl-1*H*-1,2,3,4-tetrazol-5-yl)sulfanyl]methyl}phenyl)sulfanyl]ethyl phenylcarbamate;

2-[(3-{[(4,5-diphenyl-1*H*-imidazol-2-yl)sulfanyl]methyl}-2-methylphenyl)sulfanyl]ethyl phenylcarbamate;

2-({3-[(3*H*-imidazo[4,5-*c*]pyridin-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate;

2-({3-[(1,3-benzoxazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl phenylcarbamate;

2-({2-methyl-3-[(2-pyridinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate;

2-({2-methyl-3-[(4-pyridinylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate;

2-[(2-methyl-3-{[(4-phenyl-1,3-thiazol-2-yl)sulfanyl]methyl}phenyl)sulfanyl]ethyl phenylcarbamate;

2-({2-methyl-3-[(1,3-thiazol-2-ylsulfanyl)methyl]phenyl}sulfanyl)ethyl phenylcarbamate;

2-[(3-{[(5-methoxy-1*H*-benzimidazol-2-yl)sulfanyl]methyl}-2-methylphenyl)sulfanyl]ethyl phenylcarbamate;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-*N'*-phenylurea;

N-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethyl]-*N'*-(2-pyrazinyl)urea;

6-[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]-3-nitroimidazo[1,2-*b*]pyridazine;

2-[(2-methyl-3-{[2-(2*H*-1,2,3,4-tetrazol-2-yl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole;

2-[(2-methyl-3-{[2-(2*H*-1,2,3,4-tetrazol-2-yl)ethyl]sulfanyl}benzyl)sulfanyl]-3*H*-imidazo[4,5-*c*]pyridine;

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1*H*-benzimidazole;

2-({2-methyl-3-[2-(4-morpholinyl)ethoxy]benzyl}sulfanyl)-1*H*-benzimidazole;

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1*H*-indole;

2-[(3-{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}-2-methylbenzyl)sulfanyl]-1*H*-benzimidazole;

2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-yloxy)benzyl]sulfanyl}-1*H*-benzimidazole;

2-{[3-({2-[2-(2-methoxyethoxy)ethoxy]ethyl}sulfanyl)-2-methylbenzyl]sulfanyl}-1*H*-benzimidazole;

2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazole;

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1,3-benzothiazole;

2-[(3-isobutoxy-2-methylbenzyl)sulfanyl]-1,3-benzoxazole;

2-{[3-(isobutylsulfanyl)-2-methylbenzyl]sulfanyl}-1*H*-benzimidazole;

2-[(2-methyl-3-{[2-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole;

2-[(2-methyl-3-{[2-(1*H*-1,2,4-triazol-1-yl)ethyl]sulfanyl}benzyl)sulfanyl]-1*H*-benzimidazole;

ethyl 2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazole-5-carboxylate;

1-(2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazol-5-yl)-1-propanone;

2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazol-5-amine;

(2-{[2-methyl-3-(3,6,9,12,15-pentaoxahexadec-1-ylsulfanyl)benzyl]sulfanyl}-1*H*-benzimidazol-5-yl)methanol;

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methoxyphenoxy}-1-ethanol;

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methoxyphenoxy}ethyl phenylcarbamate;

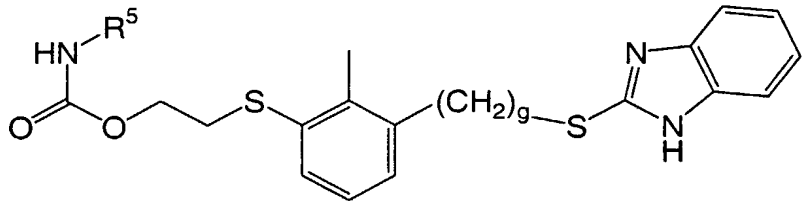
2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}-1-ethanol; and

2-{3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-chlorophenoxy}ethyl phenylcarbamate;

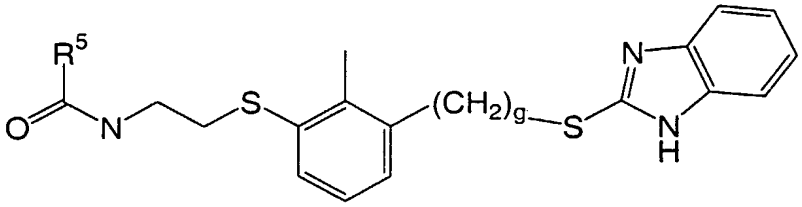
N-{[2-({3-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-2-methylphenyl}sulfanyl)ethoxy]carbonyl}phenylalanine;

or a pharmaceutically acceptable salt or solvate thereof.

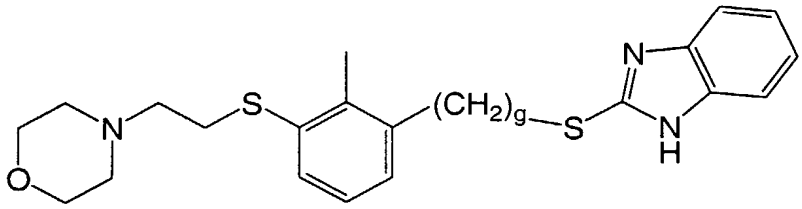
11. A compound according to Claim 1, wherein the compound is selected from compounds II, III, IV and V



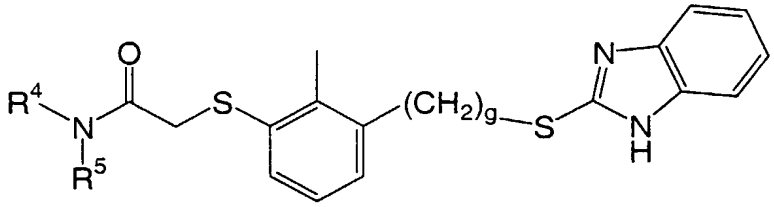
II



III



IV



V

wherein,

For R^4 and R^5, either:

(i) R^4 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; Z^2-(C_{1-8}alkyl)aryl, wherein Z^2 represents O or a bond, and the aryl is C_{6-10}, optionally substituted and optionally fused to a C_{5-10} heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted C_{6-10}aryl; an optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2 or 3 heteroatoms independently selected from O, N and S; (C_{1-8}alkyl)-R, wherein R represents an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring

structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted -C(=O)O(C_{1-8}alkyl); optionally substituted -C(=O)O-phenyl; optionally substituted -C(=O)(C_{1-8}alkyl); optionally substituted -C(=O)-phenyl; or -NHC(=O)R^6; and

R^5 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10} and optionally substituted; optionally substituted C_{6-10}aryl; or an optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or

(ii) the structure -NR^4R^5 represents a C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S and optionally fused to a C_{6-10}ring structure, -NR^4R^5 being optionally substituted.

12. A compound according to any one of Claims 1 through 11 for use as a medicament.

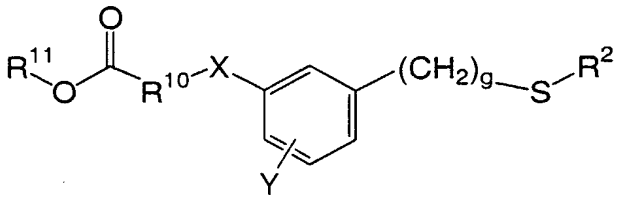
13. A pharmaceutical formulation comprising a compound according to any one of Claims 1 through 11 and a pharmaceutically acceptable diluent or carrier.

14. Use of a compound according to any one of Claims 1 through 11, in the manufacture of a medicament, for the therapeutic and/or prophylactic treatment of *Helicobacter pylori* infection in a mammalian host.

15. A method of therapeutically treating and/or preventing *Helicobacter pylori* infection in a mammal, comprising administering to the mammal a compound according to any one of Claims 1 to 11.

16. A process for preparing a compound according to Claim 1, wherein the process comprises the steps of:

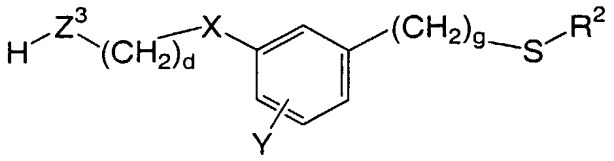
(a) reducing compound VI



VI

wherein R^{10} represents $(CH_2)_d$ or $-(CH_2)_{f-1}$-O-$(CH_2)_e$- and R^{11} represents H or C_{1-6}alkyl; or

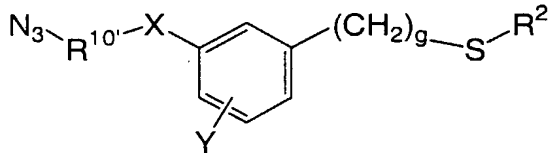
(b) reacting compound VII with R^6-NCO



VII

wherein Z^3 represents O or NH; or

(c) reducing comound VIII

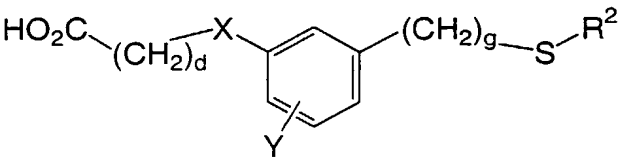


VIII

wherein $R^{10'}$ represents a bond, $(CH_2)_d$ or $-(CH_2)_f$-O-$(CH_2)_e$-; or

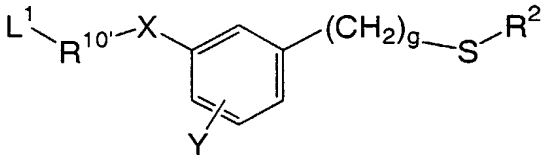
(d) reacting compound VII with R^6-COOH; or

(e) reacting compound IX with NHR^4R^5; or



IX

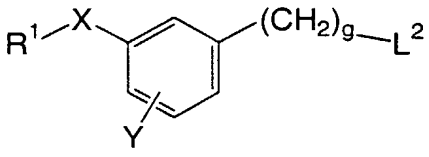
(f) reacting compound X with NHR^4R^5



X

wherein L^1 represents a leaving group and $R^{10'}$ represents $(CH_2)_d$ or $-(CH_2)_f$-O-$(CH_2)_e$-; or

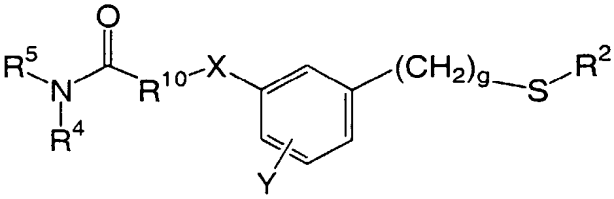
(g) reacting compound XI with R^2-SH



XI

wherein L^2 represents a leaving group; or

(h) reducing compound XII



XII

wherein,

For R^4 and R^5, either:

(i) R^4 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; Z^2-(C_{1-8}alkyl)aryl, wherein Z^2 represents O or a bond, and the aryl is C_{6-10}, optionally substituted and optionally fused to a C_{5-10} heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted C_{6-10}aryl; an optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2 or 3 heteroatoms independently selected from O, N and S; (C_{1-8}alkyl)-R, wherein R represents an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; optionally substituted -C(=O)O(C_{1-8}alkyl); optionally substituted -C(=O)O-phenyl; optionally substituted -C(=O)(C_{1-8}alkyl); optionally substituted -C(=O)-phenyl; or -NHC(=O)R^6; and

R^5 is H; C_{1-8}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10} and optionally substituted; optionally substituted C_{6-10}aryl; or an optionally substituted 5-, 6-, 7-, 8-, 9- or 10-membered heterocyclic ring structure containing 1, 2 or 3 heteroatoms independently selected from O, N and S; or

(ii) the structure -NR^4R^5 represents a C_{3-8}heterocyclic ring optionally containing 1, 2 or 3 further heteroatoms independently selected from O, N and S and optionally fused to a C_{6-10}ring structure, -NR^4R^5 being optionally substituted;

R^6 is H; C_{1-12}alkyl; optionally substituted C_{3-8}cycloalkyl optionally fused to a benzo ring; optionally substituted (C_{1-8}alkyl)aryl wherein the aryl is C_{6-10}; optionally substituted (C_{1-8}alkyl)R, where R represents a mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S or R represents a mono-, bi- or tri-cyclic C_{3-13}cycloalkyl; optionally substituted C_{6-10}aryl; an optionally substituted mono- or bi-cyclic 5-, 6-, 7-, 8-, 9- or 10-membered heterocycle containing 1, 2, 3, 4, 5 or 6 heteroatoms independently selected from O, N and S; or -C(=O)-O-Ar, wherein Ar represents optionally substituted C_{6-10}aryl; and

R^{10} is $(CH_2)_d$ or $-(CH_2)_{f-1}$-O-$(CH_2)_e$-.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 00/02192

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: C07D 235/28, A61K 31/4184, A61P 1/04
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0251536 A1 (FISONS PLC), 7 January 1988 (07.01.88) --	1-16
X	EP 0204215 B1 (G.D. SEARLE & CO.), 10 December 1986 (10.12.86) --	1-16
A	US 5576341 A (MITSUO MASAKI ET AL), 19 November 1996 (19.11.96) --	1-16

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 March 2001	14 -03- 2001
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Carolina Gómez Lagerlöf/EÖ Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE00/02192

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **15**
because they relate to subject matter not required to be searched by this Authority, namely:

see next sheet

2. ☒ Claims Nos.: **1-2**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see next sheet

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Box I.1

Claim 15 relates to a method of treatment of the human or animal body by surgery or by therapy/a diagnostic method practised on the human or animal body/Rule 39.1(iv). Nevertheless, a search has been executed for this claim. The search has been based on the alleged effects of the compound/composition.

Box I.2

Present claims 1-2 relate to an extremely large number of possible compounds. In fact, the claim contains so many variables that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the whole scope of the claims impossible.
Consequently, the search has been carried out for those parts of the application which appear to be clear and concise, namely mainly the compounds claimed in claim 10.

INTERNATIONAL SEARCH REPORT

Information on patent family members

25/02/01

International application No.
PCT/SE 00/02192

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0251536 A1	07/01/88	AU 7465487 A	07/01/88
		DK 319387 A	25/12/87
		FI 872774 A	25/12/87
		GB 8615416 D	00/00/00
		IL 82965 D	00/00/00
		JP 63005082 A	11/01/88
		NO 872625 A	28/12/87
		NZ 220770 A	26/02/90
		PT 85153 A,B	01/07/87
		ZA 8704446 A	27/04/88
		GB 8615417 D	00/00/00
		GB 8615418 D	00/00/00
		GB 8615419 D	00/00/00
		GB 8702683 D	00/00/00
		GB 8702685 D	00/00/00
		GB 8702686 D	00/00/00
EP 0204215 B1	10/12/86	AU 5768886 A	27/11/86
		JP 7103110 B	08/11/95
		JP 61293975 A	24/12/86
		US 5869513 A	09/02/99
		ZA 8603859 A	29/07/87
US 5576341 A	19/11/96	DE 69404200 D,T	08/01/98
		EP 0621035 A,B	26/10/94
		ES 2104223 T	01/10/97
		JP 6298611 A	25/10/94
		JP 8099808 A	16/04/96